NORMAL MANDIBULAR MORPHOLOGY

OF INBRED MOUSE STRAINS

by

Michelle Halum Edwards

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Jeffrey A. Dean

James K. Hartsfield

Paul L. Jamison

Richard E. Ward

Eric T. Everett

Chair of Committee

Date: ______________________

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TABLE OF CONTENTS

LIST OF ILLUSTRATIONS

INTRODUCTION

Before the inception of theme parks and movies focusing on the cartoon images of Mickey and Minnie Mouse, mice have entered the cultures of people's lives. The house mouse has lived in close association with humans since the dawn of civilization about 10,000 years ago.[1] Nomadic hunters and gatherers began to cultivate plants and domesticate animals as a means of sustenance. Mice began their relationship with human kind with the advent of farming that necessitated permanent shelters for livestock and dry food.[1] Mice were stowaways as people began to spread around the world in search of new lands. Mice are the second most successful mammalian species on earth today due to their tiny size, agility, speed, and their ability to eat almost anything.[1]

By the 19th century, the house mouse became an "object of fancy" all over the world.[1] The fondness for unusual-looking mice by the Chinese and Japanese led Asian breeders to select and develop unusual varieties of mice with strikingly different coat colors. In 1900, a retired schoolteacher, Abbie Lathrop, began to breed mice for sale as pets from her home in Granby, Massachusetts. She was able to supply early mouse geneticists such as William Castle of Harvard University and Leo Loeb of University of Pennsylvania with a constant supply of different fancy mice for their experiments. Many common inbred lines so important today are derived from animals provided by Lathrop.[1]

Inbred mouse strains represent genetically homogenous groups of individuals. Mice in one strain are often remarkably different from mice in other inbred strains. Those phenotypic differences make mice exceptional tools for the dissection of genetic factors that govern normal and abnormal craniofacial morphogenesis. Even though the molecular events that underlie craniofacial development and morphogenesis are not fully understood, it is well accepted that their orchestration is under genetic and environmental control. Animal models, including laboratory mice, have become instrumental in advancing our understanding of normal and abnormal craniofacial development mechanisms. Linkage studies and detailed mapping of mouse genes have allowed scientists to uncover regions of mouse chromosomes that show linkage and similar gene order with various segments of human chromosomes.[2] Thus, studies involving mice are a good way to understand similar processes in humans. By understanding normal craniofacial differences between genetically unrelated strains, knowledge of the mechanisms involved in craniofacial development have the potential to be more adequately understood. While numerous investigations have focused on abnormal morphogenesis, comprehensive studies of normal craniometric morphology across multiple inbred strains of mice are infrequent. A major center for mouse genetics is The Jackson Laboratory located in Bar Harbor, Maine. This non-profit laboratory was opened in 1929. The Jackson Laboratory initially bred many different species (including dogs, rabbits and guinea pigs), but it now focuses on the mouse.[1] The laboratory serves the worldwide community of mouse geneticists in three capacities. These are: 1) maintenance and distribution of hundreds of special strains and mutant stocks, 2) housing a central database resource, and 3) providing education in mouse genetics and programs for non-scientists, high school and college students, and for conferences of established investigators.

Mice are used so much in science, because they are excellent hosts for genome manipulation and have been used in many genetic studies, such as in the biomedical fields of immunology and cancer research. Mice are the smallest mammals known. Mice can be economically raised in small facilities and have relatively short life spans (1 to 3 years). Females breed prolifically (about 5 to10 pups per litter) and can have several litters in one lifetime. Simple husbandry characteristics are conducive for large-scale studies.[1]

A critical resource for biomedical research is a comprehensive data profile of normal phenotypes and genotypes of inbred strains of mice. The synteny and sequence of mouse and human genomes are remarkably similar, which validates the mouse as an exceptional model for understanding human biology.[2] Such a profile could help develop strategies that could alleviate a genetically determined condition or apply to risk assessment, diagnosis, prevention, or other treatment options for the trait of interest.[2] Knowing the genetic factors determining facial shape may lead to a better understanding of the morphogenesis of craniofacial structures and may help people understand more about normal growth and development, as well as common birth defects.

The Mouse Phenome Project, an international collaboration of investigators, was formed in May 2000 to systematically phenotype a collection of normal inbred mouse strains. This project is a component of the Mouse Phenome Project designed to collect normal craniometric data from 12 genetically homogeneous inbred strains utilizing digital images from equal numbers of female and male mice at 7 to 8 weeks of age. A consensus emerged that knowing the phenotypes of different inbred mouse strains would provide a great resource to identify new or better mouse models at the outset of a study.[2]

This would help optimize strain selection for experimental design.[3]

We hypothesize that morphometric analysis of craniofacial structures from genetically disparate inbred mouse strains will reveal quantifiable differences. These differences will in turn allow us to identify a subset of traits that will discriminate and classify the strains and set the stage for future genetic studies that will search for genes that contribute to craniofacial form.

Thus, the objectives of this research are to: 1) determine and measure differences in discrete and quantitative craniometric variables among different inbred mouse strains, and 2) assess elements of sexual dimorphism through bilateral measurements of the hemi-mandibles. It will be through careful morphometric analysis of craniofacial structures between inbred strains of mice that quantifiable differences will be identified.

We anticipate that following analyses of the mandibular traits, a subset of traits will be identified as being able to discriminate individuals between and within strains. Ideally, this subset of traits will form the cornerstone for future genetic studies. Those genetic studies will investigate, through quantitative trait loci (QTL) mapping, regions of the mouse genome that contribute to normal variation in craniofacial development and morphogenesis and serve as a first step in furthering our understanding of the genetic and environmental components that determine craniofacial form.

REVIEW OF LITERATURE

LABORATORY MICE

Craniofacial development and morphogenesis is determined by genetic and environmental factors.[4] Much of our knowledge of the mechanisms and pathways involved in craniofacial development and morphogenesis comes from the study of craniofacial disorders. Animal models, particularly the laboratory mouse, have been instrumental in advancing our understanding of normal and abnormal mechanisms of craniofacial development.[4-7] The intrinsic value of the laboratory mouse as a model stems from a number of reasons including: linkage studies, availability of a dense and detailed genetic map that makes gene mapping in mice practical and efficient; synteny or the genomic conservation of gene order with humans (regions of many mouse chromosomes show conservation of both linkage and gene order with various segments of human chromosomes), and high degrees of homology with human gene sequences.[8-10] In addition to the large number of available mutants and inbred strains, mice are excellent hosts for genome manipulation (transgenic and gene inactivation via gene targeting and homologous recombination). Finally, from a practical standpoint, mice can be easily and economically raised in relatively small facilities and have a short gestation and life span allowing large-scale and longitudinal studies to be performed. Due to the homozygous feature of inbred strains of mice, they lack the buffering effects of heterozygosity at multiple loci. Thus, they are more likely to exhibit extremes of phenotypic variation, a characteristic that offers considerable experimental potential.[3]

To fully exploit the power of mouse genetics, phenotypic and genetic diversity among inbred strains must be in the form of detailed information. Few strain surveys have been carried out for phenotypes of biological importance, and the information that does exist is fragmentary.[3] Knowing the phenotypes across multiple inbred strains would be very valuable in expanding the understanding of the mouse as an experimental organism and facilitates making a selection of the optimum strains for experimentation.[3] A strength of the mouse as a model system is the availability of inbred mouse strains. There is a wealth of inbred strains to study any phenotype of interest. Efficient use of the information gained as well as recognizing and maintaining their diversity is paramount.[11]

Repeated mating of full-siblings will produce an inbred mouse strain. The operational definition of an inbred strain is "all the descendants of a single brother-sister pair of mice produced by 20 or more generations of full-sibling inbreeding." At 20 generations, the probability of heterozygosity at any unselected locus is less than 0.02. In other words, on average, at least 98.6 percent of the loci in each mouse are homozygous.[11] Four factors contribute to the genetic divergence among inbred strains. The first is the initial heterozygosity in the common ancestral population. The second is the residual heterozygosity after n generations of inbreeding. The third is the contamination from outcrossing, and finally, heterozygosity introduced by new mutations.[12]

Mouse genetics is a field that is dependent upon data collected by any one scientist and integrated into a large-scale system of databases. In order for information to be shared among mouse geneticists, they must speak the same language. The International Committee on Standardized Nomenclature has defined this language for mouse nomenclature since 1939. This committee establishes and updates rules and guidelines for genetic nomenclature that is published regularly in *Mammalian Genome.*[1]

Original inbred mouse strains were named for a variety of reasons. For example, the BALB/c strain was named by combining the investigator's name, Bagg, with the pigment status of the mouse, which is albino. Therefore, Bagg's ALBino became BALB. Abbie Lathrop's female No. 57 gave rise to C57BL/6 and C57BL/10.[1]

The strain symbol followed by a slash (/), and a substrain symbol indicates a substrain. For example, DBA/2. Substrains arise when two or more strains of established inbred strains are isolated from each other for a long enough period of time to detect genetic differences. Specifically, one of the following three situations occur: 1) an inbred strain is separated before the F_{40} generation when residual heterozygosity is still likely; 2) an inbred strain has been separated for 100 or more generations; and 3) when genetic differences are uncovered caused by residual heterozygosity at the time of branching, mutation or contamination.[1]

A laboratory registration code is often included in the substrain name. For example, C57BL/6J is a substrain of C57BL, indicated by the /6, and the J indicates the strain is maintained by the Jackson Laboratory.[1]

An investigator can choose a new name and symbol for a locus. Nomenclature for mouse genes, alleles, and strains follow the rules and guidelines established by the International Committee on Standardized Genetic Nomenclature for Mice and is provided through the Mouse Genomic Nomenclature Committee.[13]

MOUSE PHENOME PROJECT

The Mouse Phenome Project is an international collaboration headed by an eleven-member Steering Committee in both the academic and corporate sectors. This community-wide project originated from the Strain Characterization Workshop at The Jackson Laboratory in May 1999.[3] The overwhelming consensus of workshop participants was that comprehensive phenotypic information on inbred mouse strains is urgently needed. This is because the laboratory mouse, with its hundreds of inbred, specialized and mutant strains, serves as the primary animal model for exploring genetic variation and human biology.[3] Reliable phenotypic data are essential for realizing the full utility of genomic information that will emerge from sequencing the mouse genome. The scope of this large-scale collaborative project requires international cooperation with academic and industrial participation. Experts in diverse fields of biomedical science were invited to generate this phenotypic data. A central web-accessible database for the archiving and management of these data has been developed and housed at The Jackson Laboratory, so that the data can be integrated with the Mouse Genome Database.[3]

With the advancement of molecular genetic tools, it will be possible to look for genes underlying the quantitative traits of murine craniofacial morphogenesis. Improved understanding of the genetic influences on facial shape may lead to a better understanding of differences in craniofacial morphology. This in turn may increase the factors that may predispose people to common human birth defects (e.g., cleft lip and cleft palate), and clinical asymmetries affecting craniofacial and dental structures.

CRANIOFACIAL DEVELOPMENT IN HUMANS AND MICE

Diewert and Wang[14] have shown that human and mouse embryos have similar stages, yet timing is not the same in primary palate development. In human and mouse embryos, a nasal fin forms, then a mesenchymal bridge develops through the nasal fin and rapidly enlarges, leading to primary palate formation.[14] Morphometric analyses of craniofacial growth in cleft lip and noncleft lip mice have been conducted.[14,15] Facial shape appears to be a causal factor in genetic predisposition to cleft lip in mice. Hypoplasia of one of the facial prominences is also a factor in clefting.[16] Trasler and Machado[17] found a particular facial complex associated with a cleft lip predisposition. The premaxilla length was the most discriminating trait between cleft and noncleft strains of mice. The premaxilla length was shorter in the cleft lip mice than noncleft. Also, the premaxilla width was narrower in cleft lip mice. Other contributing factors were the length of the nasal bones and the interorbital distance.[17] Differences in craniofacial shape have been observed in numerous normal and mutant mice; the most obvious was between C57BL/6J and A/J strains.[16,17] The growth of the facial processes differed between the A/J strain, (which has a 12 percent frequency of cleft lip), and C57BL, a strain that virtually never has cleft lip. In the A/J strain, the medial nasal processes do not diverge laterally as much as a strain that is not predisposed to cleft lip.[16]

Genetic models have been created to help answer questions of how morphological structures arise historically and developmentally, as well as how these structures are inherited and how they function and change over time. Atchley suggests, "The evolution of morphology is actually the evolution of the developmental processes that underlie morphology."[18]

In humans, five stages in craniofacial development are recognized: 1) germ layer formation and initial organization of craniofacial structures; 2) neural tube formation and initial formation of the oropharynx; 3) origins, migrations, and interactions of cell populations, especially neural crest cells and their derivatives; 4) formation of organ systems, especially the pharyngeal arches and the primary and secondary palates; and 5) final differentiation of tissues (skeletal, muscular, and nervous elements).[19]

During human development, the lower jaw is formed from the mandibular component of the first branchial arch. The mandibular processes are bilaterally symmetrical structures located below the future oral cavity. These processes are composed of mesenchymal tissue enclosed by an epithelial layer of ectodermal and endodermal origin. The mesenchyme of the mandibular processes is derived from neural crest cells.[19]

After the initial formation in humans, the processes grow along three axes, come together in the midline, and give rise to a triangular-shaped lower jaw. Mandibular processes fuse together at the lateral corners with the maxillary processes and at their lower borders with the hyoid process, in addition to coming together in the midline or symphyseal region.[20] Interplay among chondroblasts, fibroblasts, osteoblasts, and myoblasts as well as their derivative tissues, together with neural and vascular tissue and teeth, will determine mandibular form in interaction with environmental factors.

The greater part of the mouse mandible is composed of a single bone, the dentary. The body of the dentary and the basal portion of the condylar process results from intramembranous ossification. Secondary cartilages appear on the dermal bone at the future sites of the condylar, coronoid, and angular processes. These secondary cartilages, through endochondral ossification, will serve an important role in the growth of the ramus of the mouse mandible.[21]

Skeletal growth and morphogenesis have often been described as being “intrinsic” or “extrinsic” in origin, similar to the discussion of nature versus nurture. Intrinsic factors are involved with programming tissue-specific morphogenesis and generating the individual skeletal elements.[21] Extrinsic refers to influences on individual skeletal elements arising from adjacent developing tissues (muscles, nerves, blood vessels, teeth, and connective and skeletal tissue).[21] However, growth and development are not the result of genetic and environmental (non-genetic or epigenetic) factors working in total absence or independence of each other. Biomechanical and biophysical factors, as well as hormones and functional matrices influence final form and size of the craniofacial skeleton by acting in conjunction with intrinsic factors.[21]

SEXUAL DIMORPHISM

Sexual dimorphism occurs when there are differences in the male and female body due to sexual maturation and includes secondary sex characteristics. Sex hormones can effect gene expression leading to sexual dimorphism. In the third week of life, a young mouse resembles an adult mouse except for size and sexual differentiation. The onset of puberty in a mouse is marked when ovulation first occurs in the female and when males achieve full spermatogenic activity. Inbred females first ovulate between 6 and 8 weeks of age. However, environmental factors have an effect on the timing. For example, exposure to adult males or their urine can spur the onset of ovulation. The onset of male puberty in most laboratory strains occurs about 5 weeks after birth.[1]

The role of androgens on the sexual dimorphism of mandible shape was investigated in mice carrying the X-linked gene for testicular feminization (Tfm).[22] Tfm is known to determine a profound insensitivity to testosterone and is associated with a severe reduction in androgen receptor levels in Tfm/Y males. Tfm carrier males would be expected to have the same mandible shape as females. Males affected by this mutation fail to fully sexually differentiate, exhibit female external characteristics, and are sterile. Mandible shape analysis in an inbred strain of mice showed that sexual dimorphism was observed. Androgens are involved in the mandible shape's sexual dimorphism and play a role in mandibular development in both males and females.[22]

Vogl et al.[18] compared morphological differences of two inbred strains of mice (C3HeB and C57/BL) over postnatal age. Six areas of the mandible were studied. The areas were the angular, condylar, coronoid, masseter, posterior alveolar, and anterior alveolar areas.[18] Their results indicated that morphological differences of discriminate traits change during development. Most notably, the lower posterior part of the mandible, the coronoid process, and the masseter area show significant differences at 10 to 25 days postnatal age. The coronoid process at 20 days had no significant difference. It was suggested that morphological differences in strains is not the result of a smooth and continuous process. Morphologic differences between strains may appear at one age, disappear, and reappear later at the next age. The unpredictable pattern of the development of the mandible is expected if it is integrated by epigenetic and regulatory processes.

Sexual dimorphism varies in both magnitude and pattern among species. In extinct species, craniofacial remains offer information about body-size dimorphism. Craniofacial remains that are most commonly preserved are teeth, jaws and skulls.

Primates show general patterns of greater dimorphisms in length rather than breadth and greater facial versus neurocranial and orbital dimensions.[23] Different craniofacial dimensions can reveal different size dimorphism within any species. Hominoids show less facial dimorphism than other primates.[23]

Genetic and other indirect effects arising from the interaction among other tissues affects morphology. An example of indirect effects is the mouse maternal genotype that includes uterine litter size. Maternal effects arise from the interplay between progeny and their uterine and postnatal nursing environments. The mother has the potential to modify the expression of genes in her progeny.[24] For example, tail length and body weight can be affected. In the study by Cowley et al.,[24] uterine effects were a significant influence at all ages (from birth up to 70 days of age) on both body weight and tail length. There have been other reports suggesting that uterine effects on body weight disappear after about 2 weeks of age.[25]

INDIRECT EFFECTS ON MORPHOLOGY OF MURINE CRANIOFACIAL STRUCTURES

The interactions among bone, muscle and teeth in the human mandible are also an example of indirect effects. Moss' Functional Matrix Theory explains that stimuli coming from the growth and the actions of multiple sources within the growing head and body directly, or indirectly function to turn on or off cellular activity. Thus, growing and changing custom-fitted bones are constantly accommodating the changing developmental conditions to make an interrelated system.[26]

In late prenatal and postnatal mandibular growth and morphogenesis, the development of the secondary cartilages and their effect on the mandibular processes is adaptive and depends on muscle development and activity. This extrinsic biomechanical factor could allow for phenotypic variability due to environmental rather than genetic factors.[21] Changes in the shape of the mandible during vertebrate evolution have been toward greater functional efficiency and specialization due to diet and behavior.[27] These changes include modifications in the size, shape, and location of teeth on the mandible and various processes that provide leverage and muscle attachment.[27]

The mechanical loading of muscles on bones at the site of attachment influences skeletal morphology. The face and mandible exhibit more differences in later growth, because of the increased influence of muscles on these regions as growth continues. Lightfoot and German (1998) studied the effects of muscle degeneration on craniofacial growth using two strains of muscular dystrophic mice. The severely dystrophic mice have flatter, more elongate skulls and mandibles than those strains with less severe dystrophy.[28]

In mice, masticatory development occurs sometime after birth. Infant mice suckle using the muscles of the tongue, cheeks, lips, soft palate, and pharynx. When mice begin to eat solid food, their power stroke of mastication is larger. Therefore, muscular forces that manipulate bone growth are not achieved until later.[24] Mandibular shape was compared among four different inbred strains of mice that were based on animals fed soft as opposed to hard diets. Animals maintained on a hard diet showed a greater intrastrain contrast as opposed to animals fed soft diets. This study implicated a role for muscular stimulation interacting with different genomes in influencing mandibular shape as well as size. There is much experimental evidence that reduced muscular function is associated with altered mandibular form. The role of genetic and environmental factors confirmed their influence on mandibular outline form.[29]

Maternal effects are complex interactions that may take place from the interaction between progeny and their uterine and postnatal nursing environments. Uterine and other environmental effects in addition to genotype can influence the phenotype of progeny at any age. Although genotype and postnatal factors have been shown to vary as organisms develop, little is known about the effects of uterine genotype on complex and varying traits such as skeletal dimensions. Uterine genotype is defined as the genotype of the female in which the embryo develops. The trait under consideration varies with the uterine genotype and the genotype of the progeny, and whether inbred or hybrid lines are considered. For example, considering body weight in an inbred strain, uterine effects are more important than progeny genotype from birth to 35 days. Thereafter, progeny genotype has a greater influence.[24]

WEIGHT AS AN INDICATOR OF SIZE

Body weight is considered a component of size. Scaling relations are correlated between skeletal dimensions and body size, including skeletal structures, soft body tissues, and physiological processes that are dependant on body size.[30]

MATERIALS AND METHODS

This animal study was conducted and analyzed in a manner such that the co-investigator was blinded to the sex and strain of each mouse examined. This study is a component of the global Mouse Phenome Project. The investigation included a number of quantitative morphologic traits to look at the differences in mandibular morphology within and between these strains. The goal of this study was to establish baseline phenotypic data on commonly used and genetically diverse inbred mouse strains.

PREPARATION OF MANDIBLES

Ten male and 10 female mice at 7 to 8 weeks of age when received were euthanized. Following euthanasia, each mouse was weighed and assigned a unique number. The heads were cleaned of skin, fur, loose musculature, and the tongues were removed. The heads were soaked in 1 to 2 percent sodium hypochlorite (5.25 to 6.0 percent sodium hypochlorite/0.9 percent w/v NaCl that is diluted 1:3 in 0.9 percent NaCl) for 14 to 16 hours at room temperature. The cleaned skulls were thoroughly rinsed in fresh 0.9 percent NaCl and allowed to air dry (2 to 3 days) prior to varnishing with clear polyurethane spray. The hemi-mandibles were varnished as well with no other modifications.

IMAGE PREPARATION

Both hemi-mandibles were imaged simultaneously with the buccal side facing up using a Leica GZ6 stereomicroscope equipped with a Nikon DX1200 digital camera and Dell workstation. Each pair of hemi-mandibles was imaged along with a premeasured segment of an archwire that served as a standard for size in the same horizontal plane as the hemi-mandibles. The digital images were acquired at 3600 by 2880 pixels and saved as high-resolution jpeg files (72 pixels/inch at 50 by 40 inches image size). All images generated from skeletal (hemi-mandibles) samples were digitized using Didge software, (Image Digitizing Software, version 2.20) a digitizing program written and designed by Alistair Cullum (Department of Biology, Creighton University, Omaha, NE) to help quickly mark and record coordinates on a series of images. It was originally developed for the study of animal locomotion. Selected points, as pixels, were identified and the coordinates, (X,Y) of these points were then transferred to a Microsoft Excel spreadsheet for analysis. Basic geometry formulae were applied to determine distances and areas.[31]

The distance between two points in the plane is the length of the line segment joining the two points. If the points have Cartesian coordinates (x_1, y1) and (x_2, y2), this distance is:

$$\sqrt{(x_1 - x_0)^2 + (y_1 - y_0)^2}.$$

For use as an Excel function the formula can be written as: d = ((x_2 - x_1) ^2 + (y_2 - y_1) ^2) ^0.5

Areas of triangles were determined using Heron's formula, which finds the area of any triangle when given the lengths of its three sides (a, b, and c). The Excel function formula is written as follows: Area =SQRT(s (s-a)(s-b)(s-c)) where semi-perimeter, s = (a+b+c)/2. Breaking the polygons up into triangles and then computing the sum of the areas of the triangles that define the polygons determined areas of regular and irregular polygons.

A piece of orthodontic archwire, which has a measurable physical size, (determined using a digital micrometer accurate to 0.01 mm) was used as an internal standard for calculating lengths/distances in mm. After the image was digitized, the coordinates of points defining the arch wire as well as selected landmarks on the hemi-mandibles were located and assigned (X, Y) values as pixels. These coordinates were used in standard geometric formulae to calculate Euclidian distances between two points. The distances measured in pixels were then converted to millimeters using the internal size marker (arch wire).

MANDIBLE ANALYSIS

"A landmark is a point in two- or three-dimensional space that corresponds to the position of a particular feature on an object of interest."[32] The Euclidean distance between landmarks represents the configuration of landmark points of an object and its form.[18]

A series of 20 landmarks (FIGURE 1) were digitized and the Cartesian coordinates (X,Y) for each landmark were used to calculate 15 variables (TABLE III). Each pair of hemi-mandibles was digitized for the full suite of coordinates a minimum of two times. The X, Y coordinates for the landmarks in pixels were used to calculate the measured variables (in mm or mm^2). Many of the landmarks and variables have been previously used to assess development of the mandible in mice.[21,33-35] The mandibular variables include Euclidian distances between two points, areas of triangles, and the area of an irregular polygon.

STATISTICAL ANALYSIS

There were 20 mice per strain (an equal number of males and females), and all mice were adults between 7 to 8 weeks of age. The coordinates for each landmark were determined a minimum of twice for each image (single mouse) allowing for duplicate determination of each variable per animal. Each mouse was analyzed for a total of 15 mandibular traits, which will be referred to as variables. There were 30 mandibular variables (15 right side and 15 left side). The average differences and the within-specimen errors were also calculated. The average of the two measurements were computed and used in all subsequent analyses.

To test for strain differences and sexual dimorphism, one-way analysis of variance (ANOVA) models were performed to compare the strains and the genders separately, and by side, for mean differences in each of the measured traits. The strain-by-gender interaction was included in the ANOVAs to allow for testing between strains by gender and for testing between genders by strain. To test for direction asymmetry, one-way ANOVA models were performed to compare the left and right sides for the mean differences in each of the measured traits. All one-way interactions were included in the models to provide tests between sides overall, by gender, by strain and by each strain and gender combination. Pearson correlations defined the level of significance ($p \leq 0.05$) for comparing the hemi-mandible variables.

Each mouse accessioned into the study was weighed twice, and the mean weight to ± 0.01 gm was recorded. Body weight is considered a component of size. Body weight was ordered from smallest to largest ± 2 SEM for each strain. Consistent with this order, it was applied to all the variables measured. When body weight was surveyed within and between strains, differences were noted. For each strain, males weighed more than females ($p < 0.01$, T-test). One-way ANOVA was used to determine differences in weight between strains followed by post hoc (Tukey) range tests to identify homogenous subsets of weights.

RESULTS

Two major aspects of morphological size and shape in mouse mandibles are described including: 1) dimensionality in vertical and horizontal distance and area, and 2) sexual dimorphism.

The strains were grouped by weight in grams (FIGURE 3). Body weight was ordered from smallest to largest ± 2 SEM for each strain. There were three defined weight classes. When body weights were examined with males and females grouped together, CAST/Ei and MOLF/Ei separated from the other strains as the smallest mice in the study. The remaining strains were composed of two overlapping groups. Looking at males and females separately (FIGURE 3), a similar pattern was seen for the females. However, males alone were grouped differently. Males and females of the CAST/Ei and MOLF/Ei strains stayed separate. The MOLF/Ei and CAST/Ei inbred strains are different subspecies named *M.m. molossinus* and *M.m. castaneus*, respectively. A second middle-weighted group was composed of the A/J, DBA/2J, C57BL/6J, 129S1/SvlmJ, PERA/Ei, C57BL/10J, and SJL/J strains. Except for the SJL/J strain, which is derived from *M.m. domesticus* stock, the other members of the second group are *M.m. musculus* in origin. In this second group, the PERA/Ei (Peru-Atteck) is a wild-derived inbred strain within *Mus musculus.* A third group composed the heaviest strains and included FVB/NJ, CBA/J, BALB/cbyJ and C3H/HeJ. Members of this group are *M.m. domesticus* in origin.

DIMENSIONALITY IN HORIZONTAL AND VERTICAL DISTANCES AND AREAS

The average measurements of the hemi-mandibles as used to determine group (strain) statistics are in TABLE IV to TABLE XVIII. For all variables, strain order follows increasing body weight (FIGURES 4-18).

For ease of comparison, variables that measure vertical dimensions, horizontal dimensions and area dimensions will be discussed separately. Variables that measure the vertical dimension are 4, 5, and 16. Variables 4 and 16 are measures of mandible height. Variable 4 is posterior mandible length. Variable 16 is the height of the posterior area of the mandible. When comparing body weight with these variables across all strains, the height of the mandible is somewhat correlated with body weight. Variable 4 has a weak correlation $r = 0.269$ with weight, ($p < 0.01$), while the correlation with weight for variable 16 is greater $r = 0.582$ ($p < 0.01$). The FVB/NJ strain is grouped as a heavy weight and has a short vertical height of the posterior mandible comparable to the small strains MOLF/Ei and CAST/Ei. This is an example of a large mouse with a heavy body weight having a small skeletal variable similar to the small mice.

Variable 5 measures the incisor process height (FIGURE 8). Males and females seem to be comparable in respect to the height of the incisor process. There is no significant difference between males and females in incisor process height ($p = 0.092$). There is not much intra- or inter-strain variance in the variable that measures the width of the incisor process shown in variable 5 (FIGURE 8).

There were many more horizontal variables that were measured. These variables are 1, 2, 3, 15, 18, 20, and 21. Variables 3, 20, and 21 all measure the components of the mandible length. Variable 3 represents the greatest horizontal length of the mandible from the most posterior point of the angular process. Variables 3 and 20 are highly correlated to each other ($r = 0.930$, $p < 0.01$). The two smallest strains, CAST/Ei and MOLF/Ei, have small body weights and short mandibles. Variable 20 in MOLF/Ei is not significantly correlated to body weight ($r = 0.154$, $p = 0.52$). Variable 20 in CAST/Ei is correlated to body weight ($r = 0.469$, $p=0.037$), while size and weight are generally correlated.

Variable 1 measures the posterior horizontal length of the mandible, and variable 2 measures the anterior horizontal length of the mandible. When comparing the anterior and posterior lengths of the mandible across all strains, males have a longer posterior mandible length than females ($p = 0.001$). The anterior length of the mandible is relatively equal between males and females and is not significantly different ($p = 0.326$). Body weight correlates less with the length of the anterior mandible ($r = 0.354$, $p = 0.01$) compared to the posterior length of the mandible ($r = 0.741$, $p = 0.01$). Variables 1, 2, 3, 15, 18, 20 and 21 measure horizontal dimensions of the mandible. Variables 3, 20 and 21 (Figures 5, 16 and 17, respectively) measure the anterior-posterior length of the mandible from the angular process, the coronoid process, and the midpoint between the two processes to infradentale.

Variable 15 depicts the arch length of the posterior teeth as shown in FIGURE 11. Overall, females and males are not significantly different from each other in regard to arch length ($p = 0.892$). Comparing arch length between strains, some strains differed significantly from others. For example, looking at the larger strains e.g., (CBA/J, C3H/HeJ, FVB/NJ, BALB/cbyJ), mean arch length in BALB/cbyJ is significantly different from CBA/J ($p < 0.001$) and C3H/HeJ ($p < 0 .001$), but is not different from

FVB/NJ ($p = 1.0$). Furthermore, comparing the smaller strains (CAST/Ei and MOLF/Ei) demonstrated that their arch length is not significantly different ($p = 1.0$).

Variables 11 and 17 describe the anterior area of the mandible. Variable 11 encompasses the area of the anterior mandible and variable 17 encompasses the area between the most anterior molar tooth and the most cervical area of the superior part of the incisor. Interestingly, variables 11 and 17 are highly correlated ($r = 0 .900$, $p < 0.01$). Variables 11 and 17 are also significantly correlated to body weight ($r = 0.632$, $p < 0.01$ and $r = 0.558$, $p < 0.01$), respectively.

CAST/Ei and MOLF/Ei have the smallest posterior area of the mandible. This is illustrated in variable 19 (FIGURE 16) by noting the small posterior area of the mandible to the lowest weighted strains of CAST/Ei and MOLF/ei. The other strains seem to be comparable to each other in this dimension.

Variable 7 depicts the widest part of the condyle. Although there is considerable variation between and within strains in this dimension for males and females, their means are not significantly different from each other in this dimension. ($p = 0.088$).

SEXUAL DIMORPHISM

In TABLE IV, ANOVA was performed comparing gender within each inbred mouse strain for the right-side and left-side measurements for each variable. For each strain, the total number of times a variable was significantly different ($p < 0.05$) was recorded regardless of the side. This was also done for the left-side and right-side of the hemi-mandibles. The strain with no significant difference and therefore the least total amount of sexual dimorphism was DBA/2J. This implies that the DBA/2J males and females are alike in all of the variables measured. Only three significant differences of the variables measured were found for A/J. Again, A/J, males and females are very much alike in the variables measured. The strain with the most significant variability ($p < 0.05$) between males and females of all the strains is C3H/HeJ, with 16 significant differences between males and females. The second most variable strain between the sexes was CBA/J.

The left side was examined by itself and revealed that there are no significant differences between males and females in the DBA/2J strain. The left side had two variables that were significantly different ($p < 0.05$). The strain with the greatest variability between males and females was CBA/J, then C3H/HeJ.

The right side also showed the least significance difference ($p < 0.05$) between males and females for DBA/2J and A/J. The strains with the most variability on the right side were 129S1/SvImJ and C3H/HeJ.

Weight illustrates an aspect of sexual dimorphism where males are generally larger than females. FIGURE 3 illustrates the range in size from smallest to largest categorized by weight in grams where all the males are larger than females.

ANOVA results can be seen in TABLE V and show the variables that proved to be most often significantly different between males and females. The variable that showed no significant difference between males and females ($p < 0.05$) is variable 2, which is the horizontal length of the posterior mandible. This variable was not significantly different in the total, left side, and right side measurements of the mandible. The variable that was most often significantly different between males and females is variable 3, which is the horizontal length of the mandible measured from the angular process.

TABLES AND FIGURES

TABLE I

Inbred mouse strains [a]

A/J BALB/cByJ CBA/J C3H/HeJ C57BL/6J CAST/Ei SJL	FVB/NJ DBA/2J C57BL/10J 129S1/SvImJ MOLF/Ei PERA/Ei

[a] Inbred mouse strains used in the study. All mice were obtained from The Jackson Laboratory (Bar Harbor, ME). Strain selection was based upon criteria for participation in the Mouse Phenome Project Collaborations Program. Group A strains include: A/J; BALB/cByJ; C3H/HeJ; C57BL/6J; CAST/Ei; SJL/J; FVB/NJ; DBA/2J; and 129S1/SvImJ. Group B strains include: MOLF/Ei and PERA/Ei. Group C strains include: C57BL/10J and CBA/J. Priority Group A mice are widely used with available genetic and phenotypic information, providing useful data. Present in this strain set are C57BL/6J (the strain sequenced by the Mouse Sequencing Consortium), and strains that are progenitors in transgenesis or mutagenesis studies. Also included are strains that are progenitors of recombinant inbred, consomic, or congenic strains generally easy to maintain with good reproductive performance, genetically diverse with the inclusion of the wild-derived inbred strain CAST/Ei. Priority Group B strains are also widely used in the community; some are progenitors of recombinant inbred, consomic, or congenic strains. The priority strains CBA/J and C57BL/10J are of particular interest permitting more genetic diversity.

TABLE II

Associated landmarks of mouse mandible compared to human mandible[a]

Landmark	Mouse	Human
1	Gonion /posterior most point of angular process	Gonion / Midpoint of the contour connecting the ramus and body of the mandible
2	Inferior Gonion	
3	Antegonion	Antegonion
4	Menton /posterior most tuberosity of insertion site of mandibular transverse muscle	Menton
5	Pogonion	Pogonion
6	Infradentale	Infradentale
7	Dorso-posterior most point of incisor alveolus	
8	Incisor process	
9	Posterior most point of the diastema	
10	Dorso-anterior point of the first molar alveolus	
11	Posterior molar	
12	Dorsal most point of the coronoid process	Coronoid process
13	Posterior most point of the sigmoid	
14	Ventral most point of the sigmoid	
15	Dorsal most point of the condylar process at the junction of the articular disc	
16	Anterior most point of the condylar process	
17	Condylion	Condylion
18	Ventral most point of the condylar process at the junction of the articular disc	
19	Inferior most point of the condylar process	
20	Posterior ramus	

[a] Mouse landmarks are shown in FIGURE 1 and human landmarks are shown and labeled in FIGURE 2.

TABLE III

Descriptions of the hemi-mandible traits/variables measured in the analyses

VARIABLE	MANDIBLE TRAIT	DESCRIPTIVE CODE[a]
V1	Posterior mandible length	Euclidean distance from landmarks 1 - 4
V2	Anterior mandible length	Euclidean distance from landmarks 4 - 6
V3	Total mandible length	Euclidean distance from landmarks 1 - 6
V4	Height of ramus	Euclidean distance from landmarks 3 - 14
V5	Height at incisor region	Euclidean distance from landmarks 5 - 9
V7	Condyloid width	Euclidean distance from landmarks 15 - 18
V11	Area of anterior mandible	Area defined by the polygon formed from landmarks (3, 4, 5, 6, 7, 8, 9, 10 and 11)
V14	Area of space between angular and condyloid process	Area defined by the triangle formed from landmarks (1, 19 and 20)
V15	Arch length of posterior teeth	Euclidean distance from landmarks 10 - 11
V16	Height of posterior area of the anterior mandible	Euclidean distance from landmarks 4 -11
V17	Concavity of incisor area to most anterior molar	Area defined by the triangle formed from landmarks (8, 9, and 10)
V18	Width of most anterior portion of the ramus at a vertical height equivalent to the distal surface of the molar	Euclidean distance from landmarks 11 -18
V19	Area of posterior mandible	Area of polygon calculated from landmarks (1, 2, 3, 11, 14, 15, 16, 17, 18, 19 and 20)
V20	Length of mandible from most inferior-anterior incisor area (infradentale) to most posterior area of condyle	Euclidean distance from landmarks 6 -18
V21	Length of most inferior-anterior incisor area (infradentale) to the midpoint of the convexity of the area between the condylion and angular process	Euclidean distance from landmarks 6 - 20

[a]Landmarks are shown in FIGURE 1 upper panel

TABLE IV

Strain comparisons[a]

Strain	Total[b]	Strain	Left-side[c]	Strain	Right-side[d]
DBA/2J	0	DBA/2J	0	DBA/2J	0
A/J	3	A/J	2	A/J	1
BALB/cbyJ	4	FVB/NJ	3	BALB/cbyJ	1
FVB/NJ	5	C57BL/10J	3	FVB/NJ	2
C57BL/10J	6	BALB/cbyJ	3	C57BL/10J	3
CAST/Ei	7	CAST/Ei	4	CAST/Ei	3
PERA/Ei	7	PERA/Ei	4	PERA/Ei	3
MOLF/Ei	8	MOLF/Ei	4	MOLF/Ei	4
C57BL/6J	8	C57BL/6J	4	CBA/J	4
SJL/J	9	129S1/SvImJ	4	C57BL/6J	5
129S1/SvImJ	10	SJL/J	5	SJL/J	5
CBA/J	13	CBA/J	7	129S1/SvImJ	6
C3H	16	C3H	8	C3H	8

[a] ANOVA was performed comparing gender within each inbred mouse strain for right-side and left-side measurements for each variable. Variables are described in TABLE III.
[b] For each strain, the total number of times a variable was significantly different ($p < 0.05$) regardless of side.
[c] For each strain, the total number of times a variable was significantly different ($p < 0.05$) involving the left-side measurement.
[d] For each strain, the total number of times a variable was significantly different ($p < 0.05$) involving the right-side measurement.

TABLE V

Comparing males and females within each strain: variables which are consistently and statistically different between genders and hemi-mandible side[a]

Variable	Total[b]	Variable	Left side[c]	Variable	Right side[d]
V2	0	V2	0	V2	0
V4	3	V4	2	V4	1
V15	3	V15	2	V15	1
V16	3	V16	2	V16	1
V18	3	V18	2	V18	1
V11	4	V11	3	V11	1
V17	7	V17	5	V19	2
V19	7	V19	5	V20	2
V20	8	V20	5	V17	3
V7	11	V7	7	V7	4
V5	14	V5	10	V21	4
V21	14	V21	10	V1	4
V1	16	V1	11	V5	5
V14	22	V14	15	V14	7
V3	27	V3	18	V3	9

[a] Each variable is described in TABLE III.
[b] The number of times this variable was significantly different ($p < 0.05$) in gender comparisons for both left and right side across all strains.
[c] The number of times this variable was significantly different ($p < 0.05$) in gender comparisons for the left side of the hemi-mandible.
[d] The number of times this variable was significantly different ($p < 0.05$) in gender comparisons for the right side of the hemi-mandible.

TABLE VI

Descriptive statistics for all variables in the BALB/cByJ strain[a]

MALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	8	7.28	7.59	7.45	0.09
V1RIGHT	10	6.98	7.70	7.38	0.18
V2LEFT	10	2.94	3.37	3.20	0.14
V2RIGHT	10	2.87	3.48	3.23	0.16
V3LEFT	8	10.27	10.73	10.46	0.17
V3RIGHT	10	10.12	10.65	10.44	0.15
V4LEFT	9	4.09	4.36	4.27	0.08
V4RIGHT	9	4.32	4.43	4.38	0.04
V5LEFT	10	1.69	1.86	1.77	0.05
V5RIGHT	10	1.79	1.92	1.83	0.04
V7LEFT	10	1.67	1.96	1.84	0.09
V7RIGHT	10	1.69	1.98	1.87	0.08
V11LEFT	10	13.08	14.67	13.69	0.45
V11RIGHT	10	13.18	14.93	13.79	0.49
V14LEFT	8	2.57	2.84	2.72	0.09
V14RIGHT	10	2.33	2.71	2.57	0.14
V15LEFT	10	2.20	2.39	2.29	0.06
V15RIGHT	10	2.23	2.39	2.30	0.05
V16LEFT	10	3.59	3.79	3.68	0.06
V16RIGHT	10	3.57	3.78	3.67	0.06
V17LEFT	10	1.16	1.31	1.21	0.05
V17RIGHT	10	1.10	1.37	1.21	0.07
V18LEFT	10	5.88	6.24	6.13	0.11
V18RIGHT	10	6.03	6.32	6.19	0.09
V19LEFT	8	14.12	15.52	14.53	0.50
V19RIGHT	9	14.32	16.07	15.13	0.54
V20LEFT	10	10.89	11.34	11.11	0.13
V20RIGHT	10	10.99	11.45	11.17	0.14
V21LEFT	9	9.01	9.30	9.15	0.10
V21RIGHT	10	9.01	9.42	9.16	0.11

(continued)

TABLE VI (continued)

Descriptive statistics for all variables in the BALB/cByJ strain[a]

FEMALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	9	6.98	7.32	7.14	0.12
V1RIGHT	8	7.06	7.49	7.31	0.14
V2LEFT	10	3.03	3.43	3.23	0.12
V2RIGHT	10	2.92	3.26	3.14	0.11
V3LEFT	9	9.85	10.40	10.18	0.19
V3RIGHT	8	9.95	10.52	10.30	0.20
V4LEFT	9	4.03	4.54	4.36	0.17
V4RIGHT	10	4.21	4.64	4.43	0.12
V5LEFT	10	1.63	1.85	1.75	0.07
V5RIGHT	10	1.71	1.89	1.79	0.05
V7LEFT	10	1.87	2.10	1.99	0.08
V7RIGHT	10	1.90	2.11	1.98	0.07
V11LEFT	10	12.33	13.98	13.44	0.48
V11RIGHT	10	12.57	14.24	13.59	0.48
V14LEFT	9	2.17	2.55	2.41	0.14
V14RIGHT	8	2.33	2.59	2.46	0.10
V15LEFT	10	2.17	2.38	2.32	0.06
V15RIGHT	10	2.19	2.40	2.31	0.07
V16LEFT	10	3.44	3.72	3.62	0.09
V16RIGHT	10	3.53	3.83	3.66	0.09
V17LEFT	10	1.09	1.28	1.21	0.06
V17RIGHT	10	1.13	1.30	1.23	0.06
V18LEFT	10	5.92	6.30	6.16	0.12
V18RIGHT	10	6.00	6.32	6.22	0.10
V19LEFT	9	13.29	15.50	14.68	0.76
V19RIGHT	10	14.14	15.88	15.20	0.55
V20LEFT	10	10.72	11.39	11.18	0.23
V20RIGHT	10	10.78	11.43	11.22	0.21
V21LEFT	10	8.78	9.34	9.09	0.19
V21RIGHT	10	8.79	9.30	9.12	0.17

[a] BALB/cByJ males and females
[b] Variables are described in TABLE III.
[c] The number of individuals measured for each variable.
[d] Minimum, maximum, and standard deviation values are in mm except for variables V11, V14, V17 and V19, which are in mm^2.

TABLE VII

Descriptive statistics for all variables in the A/J strain[a]

MALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	9	6.42	7.11	6.79	0.22
V1RIGHT	5	6.63	7.19	6.84	0.22
V2LEFT	9	3.39	3.84	3.57	0.14
V2RIGHT	8	3.35	3.61	3.49	0.09
V3LEFT	10	9.70	10.84	10.25	0.31
V3RIGHT	6	10.03	10.60	10.27	0.20
V4LEFT	10	3.61	4.10	3.81	0.15
V4RIGHT	10	3.75	4.22	3.93	0.15
V5LEFT	9	1.65	1.86	1.77	0.07
V5RIGHT	8	1.70	1.88	1.80	0.06
V7LEFT	10	1.58	1.88	1.70	0.10
V7RIGHT	10	1.48	1.89	1.70	0.13
V11LEFT	9	11.74	14.20	13.19	0.82
V11RIGHT	8	11.87	14.25	13.07	0.84
V14LEFT	10	2.09	2.65	2.41	0.20
V14RIGHT	6	2.30	2.58	2.46	0.11
V15LEFT	10	2.01	2.26	2.13	0.07
V15RIGHT	10	2.02	2.25	2.12	0.08
V16LEFT	9	3.27	3.67	3.49	0.13
V16RIGHT	8	3.21	3.62	3.46	0.13
V17LEFT	10	1.03	1.26	1.17	0.06
V17RIGHT	10	1.06	1.36	1.19	0.09
V18LEFT	10	5.32	5.79	5.57	0.16
V18RIGHT	10	5.45	5.82	5.64	0.13
V19LEFT	10	10.87	13.35	12.00	0.82
V19RIGHT	9	11.55	13.27	12.55	0.59
V20LEFT	10	9.90	10.90	10.38	0.27
V20RIGHT	10	9.94	10.82	10.40	0.22
V21LEFT	10	8.26	9.12	8.67	0.24
V21RIGHT	9	8.34	8.98	8.64	0.19

(continued)

TABLE VII (continued)

Descriptive statistics for all variables in the A/J strain[a]

FEMALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	5	6.19	6.83	6.58	0.25
V1RIGHT	6	6.52	7.08	6.77	0.25
V2LEFT	10	3.34	3.75	3.55	0.12
V2RIGHT	9	2.90	3.61	3.40	0.20
V3LEFT	5	9.55	10.28	10.02	0.28
V3RIGHT	7	9.82	10.30	10.07	0.20
V4LEFT	10	3.63	4.07	3.86	0.12
V4RIGHT	10	3.66	4.02	3.88	0.12
V5LEFT	10	1.70	1.82	1.76	0.04
V5RIGHT	9	1.69	1.89	1.78	0.06
V7LEFT	10	1.46	1.82	1.67	0.12
V7RIGHT	10	1.50	1.80	1.70	0.09
V11LEFT	10	11.79	13.69	12.70	0.56
V11RIGHT	9	12.41	13.39	12.87	0.38
V14LEFT	5	2.12	2.54	2.29	0.17
V14RIGHT	7	1.75	2.36	2.16	0.20
V15LEFT	10	1.87	2.21	2.10	0.10
V15RIGHT	10	2.01	2.20	2.13	0.07
V16LEFT	10	3.30	3.47	3.41	0.07
V16RIGHT	9	3.34	3.62	3.46	0.09
V17LEFT	10	1.07	1.24	1.14	0.05
V17RIGHT	10	1.01	1.25	1.14	0.06
V18LEFT	10	5.20	5.70	5.52	0.16
V18RIGHT	10	5.35	5.78	5.61	0.14
V19LEFT	10	10.93	12.78	12.04	0.62
V19RIGHT	10	11.62	13.18	12.40	0.48
V20LEFT	10	9.92	10.60	10.29	0.21
V20RIGHT	10	10.13	10.61	10.37	0.16
V21LEFT	10	8.20	8.77	8.56	0.19
V21RIGHT	10	8.40	8.84	8.61	0.15

[a] A/J males and females.
[b]Variables described in TABLE III.
[c]Number of individuals measured for each variable. Missing values are from damaged mandibles that were missing a landmark.
[d] Minimum, maximum, and standard deviation in mm except for variables 11, 14, 17 and 19, which are in mm^2.

TABLE VIII

Descriptive statistics for all variables in the 129S1/SvImJ strain[a]

MALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	10	6.37	7.12	6.83	0.21
V1RIGHT	10	6.83	7.27	7.03	0.14
V2LEFT	10	3.89	4.12	4.00	0.08
V2RIGHT	10	3.76	4.08	3.97	0.09
V3LEFT	10	10.30	10.99	10.67	0.20
V3RIGHT	10	10.60	11.10	10.83	0.17
V4LEFT	10	4.28	4.53	4.39	0.08
V4RIGHT	10	4.34	4.64	4.46	0.09
V5LEFT	10	1.80	1.96	1.88	0.05
V5RIGHT	10	1.83	1.97	1.90	0.05
V7LEFT	10	1.66	2.08	1.92	0.13
V7RIGHT	10	1.90	2.11	2.00	0.07
V11LEFT	10	15.12	15.90	15.46	0.28
V11RIGHT	10	14.69	16.64	15.37	0.54
V14LEFT	10	2.41	2.84	2.67	0.15
V14RIGHT	10	2.41	3.01	2.72	0.20
V15LEFT	10	2.18	2.32	2.24	0.05
V15RIGHT	10	2.17	2.32	2.24	0.05
V16LEFT	10	3.64	3.81	3.72	0.07
V16RIGHT	10	3.63	3.84	3.72	0.07
V17LEFT	10	1.29	1.54	1.44	0.09
V17RIGHT	10	1.28	1.64	1.47	0.11
V18LEFT	10	5.69	6.13	5.90	0.16
V18RIGHT	10	5.74	6.24	6.02	0.18
V19LEFT	10	12.98	15.20	14.26	0.74
V19RIGHT	10	13.83	15.92	14.83	0.67
V20LEFT	10	10.84	11.43	11.13	0.19
V20RIGHT	10	10.91	11.55	11.23	0.21
V21LEFT	10	9.03	9.57	9.28	0.16
V21RIGHT	10	9.22	9.57	9.38	0.14

(continued)

TABLE VIII (continued)

Descriptive statistics for all variables in the 129S1/SvImJ strain[a]

FEMALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	9	6.49	6.96	6.77	0.15
V1RIGHT	10	6.61	6.98	6.85	0.12
V2LEFT	10	3.79	4.09	3.92	0.11
V2RIGHT	10	3.77	3.93	3.86	0.06
V3LEFT	9	10.14	10.76	10.48	0.20
V3RIGHT	10	10.19	10.70	10.51	0.16
V4LEFT	10	4.18	4.60	4.36	0.14
V4RIGHT	10	4.26	4.66	4.48	0.14
V5LEFT	10	1.71	1.92	1.82	0.06
V5RIGHT	10	1.83	1.99	1.89	0.05
V7LEFT	10	2.02	2.23	2.10	0.06
V7RIGHT	10	1.93	2.21	2.08	0.10
V11LEFT	10	13.77	15.68	14.96	0.63
V11RIGHT	10	13.73	16.08	14.90	0.77
V14LEFT	9	2.28	2.78	2.57	0.16
V14RIGHT	10	2.31	2.73	2.58	0.13
V15LEFT	10	2.09	2.34	2.18	0.08
V15RIGHT	10	2.03	2.31	2.19	0.09
V16LEFT	10	3.51	3.82	3.66	0.11
V16RIGHT	10	3.49	3.79	3.67	0.10
V17LEFT	10	1.30	1.52	1.42	0.09
V17RIGHT	10	1.30	1.50	1.40	0.07
V18LEFT	10	5.66	6.23	5.95	0.17
V18RIGHT	10	5.90	6.22	6.03	0.11
V19LEFT	10	13.88	15.90	14.64	0.70
V19RIGHT	10	14.57	16.01	15.18	0.53
V20LEFT	10	10.76	11.44	11.10	0.24
V20RIGHT	10	10.86	11.43	11.17	0.17
V21LEFT	10	8.90	9.41	9.17	0.15
V21RIGHT	10	8.97	9.42	9.19	0.14

[a] 129S1/SvImJ males and females.
[b]Variables described in TABLE III.
[c]Number of individuals measured for each variable.
[d] Minimum, maximum, and standard deviation in mm except for variables 11, 14, 17 and 19, which are in mm^2.

TABLE IX

Descriptive statistics for all variables in the C3H/HeJ strain[a]

MALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	10	6.90	7.36	7.13	0.16
V1RIGHT	10	7.08	7.60	7.23	0.16
V2LEFT	10	3.52	3.90	3.69	0.12
V2RIGHT	10	3.45	3.72	3.57	0.09
V3LEFT	10	10.55	10.85	10.69	0.12
V3RIGHT	10	10.48	10.88	10.66	0.14
V4LEFT	10	4.03	4.35	4.20	0.10
V4RIGHT	10	4.12	4.59	4.37	0.16
V5LEFT	10	1.82	1.98	1.89	0.05
V5RIGHT	10	1.84	1.96	1.91	0.04
V7LEFT	10	1.95	2.16	2.06	0.06
V7RIGHT	10	1.98	2.20	2.07	0.07
V11LEFT	10	14.56	16.38	15.05	0.56
V11RIGHT	10	13.80	15.99	14.70	0.67
V14LEFT	10	2.38	2.83	2.69	0.13
V14RIGHT	10	2.37	2.84	2.63	0.15
V15LEFT	10	1.96	2.12	2.05	0.05
V15RIGHT	10	2.02	2.17	2.09	0.05
V16LEFT	10	3.48	3.74	3.62	0.09
V16RIGHT	10	3.55	3.89	3.66	0.10
V17LEFT	10	1.29	1.55	1.38	0.08
V17RIGHT	10	1.27	1.47	1.38	0.07
V18LEFT	10	5.99	6.36	6.17	0.13
V18RIGHT	10	6.00	6.33	6.15	0.12
V19LEFT	10	14.28	16.03	15.02	0.65
V19RIGHT	10	14.79	16.85	15.54	0.69
V20LEFT	10	10.81	11.20	10.97	0.13
V20RIGHT	10	10.75	11.26	10.97	0.19
V21LEFT	10	8.98	9.36	9.15	0.11
V21RIGHT	10	8.89	9.40	9.15	0.14

(continued)

TABLE IX (continued)

Descriptive statistics for all variables in the C3H/HeJ strain[a]

FEMALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	10	6.57	6.94	6.76	0.13
V1RIGHT	9	6.46	7.09	6.86	0.22
V2LEFT	10	3.41	3.89	3.69	0.14
V2RIGHT	10	3.45	3.75	3.58	0.12
V3LEFT	10	9.90	10.64	10.29	0.20
V3RIGHT	9	9.78	10.70	10.29	0.32
V4LEFT	9	3.95	4.29	4.15	0.13
V4RIGHT	9	4.04	4.69	4.28	0.18
V5LEFT	10	1.68	1.97	1.85	0.08
V5RIGHT	10	1.75	2.01	1.87	0.07
V7LEFT	10	1.73	2.21	2.01	0.12
V7RIGHT	10	1.78	2.14	1.98	0.10
V11LEFT	10	13.32	15.69	14.67	0.69
V11RIGHT	10	12.89	16.28	14.27	0.89
V14LEFT	10	2.13	2.33	2.24	0.06
V14RIGHT	9	1.97	2.36	2.22	0.13
V15LEFT	10	1.94	2.19	2.07	0.09
V15RIGHT	10	2.03	2.21	2.11	0.06
V16LEFT	10	3.39	3.76	3.56	0.12
V16RIGHT	10	3.36	3.74	3.58	0.12
V17LEFT	10	1.18	1.49	1.31	0.10
V17RIGHT	10	1.23	1.46	1.33	0.08
V18LEFT	10	5.83	6.21	5.97	0.12
V18RIGHT	10	5.67	6.20	5.96	0.17
V19LEFT	9	13.24	15.32	14.30	0.66
V19RIGHT	9	12.99	16.48	14.63	0.94
V20LEFT	10	10.26	11.23	10.75	0.26
V20RIGHT	10	10.25	11.14	10.76	0.29
V21LEFT	10	8.61	9.31	8.98	0.22
V21RIGHT	10	8.59	9.32	8.96	0.24

[a] C3H/HeJ males and females.
[b]Variables described in TABLE III.
[c]Number of individuals measured for each variable.
[d] Minimum, maximum, and standard deviation in mm except for variables 11, 14, 17 and 19, which are in mm^2.

TABLE X

Descriptive statistics for all variables in the C57BL/6J strain[a]

MALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	9	6.56	6.96	6.77	0.13
V1RIGHT	9	6.68	6.91	6.79	0.09
V2LEFT	10	3.81	4.20	4.05	0.13
V2RIGHT	10	3.91	4.18	4.03	0.09
V3LEFT	9	10.40	10.90	10.64	0.15
V3RIGHT	9	10.42	10.93	10.65	0.16
V4LEFT	10	4.02	4.50	4.19	0.15
V4RIGHT	10	4.11	4.55	4.34	0.13
V5LEFT	10	2.01	2.16	2.07	0.05
V5RIGHT	10	2.01	2.18	2.10	0.05
V7LEFT	10	1.85	2.04	1.94	0.05
V7RIGHT	10	1.87	2.09	1.98	0.06
V11LEFT	10	14.47	15.57	15.02	0.44
V11RIGHT	10	14.35	15.49	15.02	0.35
V14LEFT	9	2.79	3.34	2.96	0.20
V14RIGHT	9	2.45	3.19	2.87	0.21
V15LEFT	10	2.19	2.36	2.28	0.05
V15RIGHT	10	2.20	2.38	2.28	0.06
V16LEFT	10	3.50	3.79	3.68	0.09
V16RIGHT	10	3.63	3.87	3.70	0.07
V17LEFT	10	1.12	1.38	1.27	0.08
V17RIGHT	10	1.22	1.44	1.30	0.07
V18LEFT	10	6.02	6.42	6.14	0.13
V18RIGHT	10	5.95	6.41	6.17	0.16
V19LEFT	10	13.44	16.42	14.43	0.94
V19RIGHT	10	14.05	16.18	15.12	0.71
V20LEFT	10	11.16	11.69	11.32	0.18
V20RIGHT	10	11.05	11.62	11.36	0.19
V21LEFT	10	8.99	9.31	9.11	0.10
V21RIGHT	10	8.94	9.28	9.16	0.12

(continued)

TABLE X (continued)

Descriptive statistics for all variables in the C57BL/6J strain[a]

FEMALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	9	6.47	6.91	6.64	0.14
V1RIGHT	10	6.52	6.89	6.68	0.13
V2LEFT	9	3.82	4.20	3.98	0.12
V2RIGHT	10	3.75	4.09	3.93	0.11
V3LEFT	10	10.17	10.71	10.42	0.18
V3RIGHT	10	10.23	10.61	10.41	0.13
V4LEFT	10	3.93	4.40	4.18	0.16
V4RIGHT	9	4.07	4.52	4.39	0.15
V5LEFT	9	1.78	2.03	1.96	0.08
V5RIGHT	10	1.92	2.11	2.00	0.05
V7LEFT	10	1.78	2.07	1.92	0.08
V7RIGHT	10	1.78	2.14	1.96	0.11
V11LEFT	9	12.68	15.17	14.41	0.80
V11RIGHT	10	13.30	15.57	14.10	0.74
V14LEFT	10	2.40	2.74	2.55	0.12
V14RIGHT	10	2.27	2.72	2.51	0.15
V15LEFT	10	2.22	2.64	2.30	0.12
V15RIGHT	10	2.20	2.40	2.28	0.06
V16LEFT	9	3.52	3.89	3.67	0.12
V16RIGHT	10	3.50	3.72	3.64	0.07
V17LEFT	10	1.12	1.40	1.24	0.09
V17RIGHT	10	1.06	1.37	1.21	0.11
V18LEFT	10	5.53	6.26	6.01	0.23
V18RIGHT	10	5.86	6.28	6.04	0.13
V19LEFT	10	12.56	15.24	14.08	0.83
V19RIGHT	9	13.58	16.14	14.72	0.81
V20LEFT	10	10.76	11.54	11.17	0.24
V20RIGHT	10	10.91	11.51	11.19	0.18
V21LEFT	10	8.66	9.30	9.02	0.19
V21RIGHT	10	8.71	9.24	9.04	0.16

[a] C57BL/6J males and females.
[b] Variables described in TABLE III.
[c] Number of individuals measured for each variable.
[d] Minimum, maximum, and standard deviation in mm except for variables 11, 14, 17 and 19, which are in mm^2.

TABLE XI

Descriptive statistics for all variables in the C57BL/10J strain[a]

MALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	7	6.51	6.75	6.59	0.08
V1RIGHT	7	6.43	6.83	6.63	0.14
V2LEFT	8	3.68	4.11	3.97	0.16
V2RIGHT	9	2.68	4.17	3.83	0.45
V3LEFT	9	10.09	10.61	10.38	0.18
V3RIGHT	8	10.12	10.80	10.48	0.20
V4LEFT	10	4.10	4.62	4.38	0.16
V4RIGHT	10	3.86	4.88	4.55	0.29
V5LEFT	8	2.04	2.27	2.13	0.07
V5RIGHT	7	2.08	2.22	2.15	0.05
V7LEFT	10	1.80	2.11	1.90	0.09
V7RIGHT	10	1.74	2.07	1.89	0.11
V11LEFT	8	14.49	16.12	15.13	0.54
V11RIGHT	7	13.93	15.63	14.85	0.66
V14LEFT	9	2.70	3.15	2.88	0.19
V14RIGHT	8	2.70	3.15	2.85	0.14
V15LEFT	10	2.31	2.44	2.37	0.04
V15RIGHT	10	2.26	2.48	2.39	0.06
V16LEFT	8	3.61	3.84	3.70	0.08
V16RIGHT	9	3.21	3.79	3.64	0.19
V17LEFT	10	1.18	1.37	1.28	0.07
V17RIGHT	10	0.80	1.39	1.23	0.16
V18LEFT	10	5.83	6.56	6.24	0.24
V18RIGHT	10	6.00	6.64	6.32	0.18
V19LEFT	10	13.00	16.96	14.92	1.25
V19RIGHT	10	14.03	16.58	15.59	0.99
V20LEFT	10	10.75	11.71	11.28	0.31
V20RIGHT	10	10.16	11.76	11.29	0.46
V21LEFT	10	8.69	9.30	9.09	0.20
V21RIGHT	10	7.87	9.45	9.05	0.47

(continued)

TABLE XI (continued)

Descriptive statistics for all variables in the C57BL/10J strain[a]

FEMALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	9	5.88	6.59	6.40	0.22
V1RIGHT	10	6.17	6.93	6.51	0.21
V2LEFT	10	3.82	4.11	3.96	0.09
V2RIGHT	10	3.32	4.00	3.82	0.20
V3LEFT	9	9.54	10.53	10.20	0.30
V3RIGHT	10	9.64	10.54	10.18	0.30
V4LEFT	10	4.17	4.74	4.40	0.20
V4RIGHT	9	4.22	4.77	4.51	0.17
V5LEFT	10	1.96	2.12	2.05	0.06
V5RIGHT	10	1.98	2.13	2.07	0.05
V7LEFT	10	1.75	2.02	1.85	0.09
V7RIGHT	9	1.64	1.98	1.84	0.11
V11LEFT	10	13.86	16.02	14.67	0.69
V11RIGHT	10	12.92	15.61	14.51	0.81
V14LEFT	9	2.28	2.90	2.60	0.21
V14RIGHT	9	2.39	2.71	2.56	0.12
V15LEFT	10	2.24	2.44	2.36	0.07
V15RIGHT	10	2.18	2.44	2.33	0.09
V16LEFT	10	3.51	3.80	3.67	0.11
V16RIGHT	10	3.40	3.88	3.66	0.15
V17LEFT	10	1.14	1.36	1.26	0.09
V17RIGHT	10	1.15	1.35	1.27	0.06
V18LEFT	10	5.86	6.32	6.14	0.13
V18RIGHT	9	5.74	6.45	6.21	0.22
V19LEFT	10	13.04	16.00	14.79	0.93
V19RIGHT	9	13.35	16.14	15.10	0.82
V20LEFT	10	10.69	11.54	11.22	0.24
V20RIGHT	9	10.51	11.57	11.15	0.31
V21LEFT	10	8.54	9.37	9.01	0.22
V21RIGHT	10	8.57	9.30	8.98	0.27

[a] C57BL/10J males and females.
[b]Variables described in TABLE III.
[c]Number of individuals measured for each variable.
[d] Minimum, maximum, and standard deviation in mm except for variables 11, 14, 17 and 19, which are in mm^2.

TABLE XII

Descriptive statistics for all variables in the CAST/Ei strain[a]

MALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	9	5.92	6.39	6.12	0.17
V1RIGHT	10	5.84	6.31	6.15	0.13
V2LEFT	10	2.67	3.08	2.90	0.14
V2RIGHT	10	2.77	3.04	2.90	0.09
V3LEFT	9	8.51	9.29	8.88	0.22
V3RIGHT	10	8.67	9.19	8.90	0.15
V4LEFT	10	3.51	3.89	3.73	0.12
V4RIGHT	8	3.62	4.06	3.80	0.16
V5LEFT	10	1.49	1.68	1.59	0.06
V5RIGHT	10	1.53	1.69	1.60	0.05
V7LEFT	10	1.61	1.90	1.79	0.09
V7RIGHT	10	1.68	1.90	1.78	0.08
V11LEFT	10	8.62	11.49	10.35	0.74
V11RIGHT	10	9.84	11.14	10.37	0.43
V14LEFT	9	1.45	1.87	1.67	0.16
V14RIGHT	10	1.41	1.80	1.63	0.12
V15LEFT	10	1.41	2.30	2.00	0.24
V15RIGHT	10	1.43	2.24	1.97	0.23
V16LEFT	10	2.76	3.38	3.21	0.19
V16RIGHT	10	2.89	3.43	3.19	0.15
V17LEFT	10	0.41	0.93	0.75	0.14
V17RIGHT	10	0.72	0.91	0.79	0.06
V18LEFT	10	4.59	5.56	5.06	0.28
V18RIGHT	10	4.81	5.74	5.11	0.25
V19LEFT	9	9.44	11.52	10.55	0.61
V19RIGHT	8	9.99	11.49	10.86	0.61
V20LEFT	10	9.12	9.84	9.32	0.22
V20RIGHT	10	9.14	9.51	9.38	0.12
V21LEFT	9	7.62	8.22	7.82	0.19
V21RIGHT	10	7.67	8.15	7.89	0.14

(continued)

TABLE XII (continued)

Descriptive statistics for all variables in the CAST/Ei strain[a]

FEMALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	8	5.80	6.27	5.97	0.15
V1RIGHT	10	5.81	6.20	5.99	0.13
V2LEFT	10	2.74	2.99	2.87	0.09
V2RIGHT	10	2.68	3.09	2.85	0.13
V3LEFT	8	8.47	9.09	8.71	0.20
V3RIGHT	10	8.49	9.01	8.70	0.17
V4LEFT	8	3.53	3.91	3.67	0.13
V4RIGHT	10	3.59	4.20	3.84	0.19
V5LEFT	10	1.47	1.59	1.53	0.03
V5RIGHT	10	1.51	1.64	1.57	0.04
V7LEFT	9	1.74	1.86	1.79	0.04
V7RIGHT	10	1.74	1.88	1.80	0.04
V11LEFT	10	8.90	11.31	10.02	0.64
V11RIGHT	10	8.54	11.12	9.87	0.73
V14LEFT	8	1.38	1.63	1.53	0.10
V14RIGHT	10	1.39	1.87	1.57	0.15
V15LEFT	10	1.59	2.23	1.94	0.21
V15RIGHT	10	1.37	2.17	1.86	0.27
V16LEFT	10	2.89	3.36	3.08	0.16
V16RIGHT	10	2.84	3.20	3.08	0.14
V17LEFT	10	0.73	0.86	0.80	0.04
V17RIGHT	10	0.70	0.95	0.80	0.07
V18LEFT	10	4.70	5.49	5.08	0.24
V18RIGHT	10	5.04	5.64	5.22	0.21
V19LEFT	7	9.72	10.94	10.20	0.52
V19RIGHT	10	10.35	12.12	11.09	0.54
V20LEFT	10	9.03	9.55	9.25	0.15
V20RIGHT	10	9.14	9.50	9.34	0.12
V21LEFT	10	7.57	8.06	7.72	0.15
V21RIGHT	10	7.56	7.87	7.76	0.11

[a] CAST/Ei males and females.
[b] Variables described in TABLE III.
[c] Number of individuals measured for each variable.
[d] Minimum, maximum, and standard deviation in mm except for variables 11, 14, 17 and 19, which are in mm^2.

TABLE XIII

Descriptive statistics for all the variables in the CBA/J strain[a]

MALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	10	6.56	7.15	6.82	0.16
V1RIGHT	10	6.53	7.09	6.88	0.20
V2LEFT	10	3.25	3.73	3.55	0.16
V2RIGHT	10	3.28	3.75	3.53	0.15
V3LEFT	10	9.85	10.62	10.23	0.24
V3RIGHT	10	9.67	10.67	10.27	0.31
V4LEFT	10	3.84	4.19	3.99	0.12
V4RIGHT	10	3.85	4.30	4.07	0.13
V5LEFT	10	1.79	2.02	1.90	0.08
V5RIGHT	10	1.78	2.03	1.93	0.08
V7LEFT	10	1.77	2.05	1.87	0.08
V7RIGHT	10	1.85	2.07	1.93	0.06
V11LEFT	10	12.65	15.31	14.35	0.80
V11RIGHT	10	12.35	15.46	14.31	0.87
V14LEFT	10	2.24	2.88	2.70	0.19
V14RIGHT	10	2.34	2.91	2.77	0.17
V15LEFT	10	1.81	2.26	2.13	0.13
V15RIGHT	10	2.04	2.26	2.14	0.06
V16LEFT	10	3.31	3.76	3.60	0.13
V16RIGHT	10	3.44	3.81	3.66	0.10
V17LEFT	10	1.06	1.23	1.15	0.05
V17RIGHT	10	1.08	1.24	1.17	0.06
V18LEFT	10	5.71	6.02	5.85	0.12
V18RIGHT	10	5.39	6.04	5.82	0.19
V19LEFT	10	12.31	14.24	13.23	0.73
V19RIGHT	10	11.84	14.70	13.63	0.93
V20LEFT	10	10.35	10.96	10.62	0.19
V20RIGHT	10	9.93	11.01	10.63	0.32
V21LEFT	10	8.35	8.85	8.66	0.19
V21RIGHT	10	8.10	8.94	8.63	0.26

(continued)

TABLE XIII (continued)

Descriptive statistics for all the variables in the CBA/J strain[a]

FEMALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	8	6.39	6.77	6.61	0.13
V1RIGHT	9	6.51	6.79	6.66	0.08
V2LEFT	9	2.89	3.70	3.43	0.23
V2RIGHT	10	3.29	3.55	3.45	0.11
V3LEFT	9	9.11	10.15	9.85	0.31
V3RIGHT	9	9.82	10.13	9.98	0.12
V4LEFT	10	3.76	4.09	3.98	0.10
V4RIGHT	10	3.91	4.19	4.02	0.09
V5LEFT	9	1.71	1.93	1.84	0.07
V5RIGHT	10	1.78	2.01	1.87	0.07
V7LEFT	10	1.77	1.99	1.89	0.07
V7RIGHT	10	1.68	1.99	1.88	0.10
V11LEFT	9	12.91	14.46	13.97	0.51
V11RIGHT	10	12.23	14.31	13.80	0.59
V14LEFT	9	2.32	2.74	2.56	0.13
V14RIGHT	9	2.59	2.79	2.66	0.07
V15LEFT	10	2.11	2.20	2.13	0.03
V15RIGHT	10	2.05	2.29	2.17	0.07
V16LEFT	9	3.58	3.75	3.65	0.06
V16RIGHT	10	3.47	3.75	3.63	0.08
V17LEFT	10	0.99	1.21	1.13	0.06
V17RIGHT	10	0.85	1.20	1.11	0.10
V18LEFT	10	5.22	5.92	5.71	0.20
V18RIGHT	10	5.24	5.90	5.73	0.19
V19LEFT	10	10.70	13.40	12.56	0.73
V19RIGHT	10	11.40	13.96	13.11	0.70
V20LEFT	10	9.67	10.65	10.40	0.27
V20RIGHT	10	9.83	10.64	10.45	0.24
V21LEFT	10	7.80	8.68	8.40	0.24
V21RIGHT	10	7.72	8.63	8.38	0.26

[a] CBA/J males and females.
[b]Variables described in TABLE III.
[c]Number of individuals measured for each variable.
[d] Minimum, maximum, and standard deviation in mm except for variables 11, 14, 17 and 19, which are in mm^2.

TABLE XIV

Descriptive statistics for all variables in the DBA/2J strain[a]

MALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	10	6.55	6.94	6.74	0.14
V1RIGHT	10	6.49	7.02	6.82	0.14
V2LEFT	10	3.02	3.36	3.20	0.10
V2RIGHT	10	2.99	3.21	3.10	0.07
V3LEFT	10	9.58	9.99	9.83	0.15
V3RIGHT	10	9.36	10.12	9.82	0.19
V4LEFT	10	3.94	4.29	4.14	0.14
V4RIGHT	10	4.10	4.76	4.29	0.19
V5LEFT	10	1.70	1.83	1.77	0.05
V5RIGHT	10	1.72	1.86	1.78	0.04
V7LEFT	10	1.44	1.84	1.66	0.14
V7RIGHT	10	1.63	1.86	1.76	0.08
V11LEFT	10	12.53	14.05	13.30	0.46
V11RIGHT	10	11.86	13.54	12.79	0.61
V14LEFT	10	2.41	2.94	2.64	0.17
V14RIGHT	10	2.49	2.85	2.64	0.10
V15LEFT	10	2.03	2.32	2.14	0.11
V15RIGHT	10	2.03	2.27	2.19	0.07
V16LEFT	10	3.28	3.61	3.44	0.11
V16RIGHT	10	3.35	3.60	3.45	0.08
V17LEFT	10	1.14	1.41	1.24	0.08
V17RIGHT	10	1.01	1.33	1.18	0.12
V18LEFT	10	5.56	5.96	5.73	0.13
V18RIGHT	10	5.54	5.84	5.70	0.10
V19LEFT	10	11.60	13.83	12.90	0.75
V19RIGHT	10	12.45	13.73	13.17	0.38
V20LEFT	10	10.23	10.75	10.49	0.15
V20RIGHT	10	10.17	10.66	10.46	0.16
V21LEFT	10	8.27	8.59	8.44	0.10
V21RIGHT	10	8.08	8.71	8.40	0.16

(continued)

TABLE XIV (continued)

Descriptive statistics for all variables in the DBA/2J strain[a]

FEMALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	10	6.49	6.86	6.70	0.12
V1RIGHT	9	5.96	6.98	6.68	0.31
V2LEFT	10	3.09	3.41	3.22	0.10
V2RIGHT	10	2.33	3.78	3.14	0.35
V3LEFT	10	9.49	10.05	9.79	0.17
V3RIGHT	9	9.09	10.03	9.69	0.28
V4LEFT	10	4.00	4.41	4.17	0.12
V4RIGHT	8	4.06	4.84	4.40	0.29
V5LEFT	10	1.71	1.84	1.76	0.05
V5RIGHT	10	1.66	1.89	1.80	0.06
V7LEFT	10	1.50	1.92	1.68	0.12
V7RIGHT	10	1.60	1.77	1.69	0.06
V11LEFT	10	12.26	13.84	13.15	0.47
V11RIGHT	10	11.13	14.27	12.50	0.98
V14LEFT	10	2.33	2.86	2.58	0.16
V14RIGHT	8	2.39	2.80	2.57	0.12
V15LEFT	10	1.98	2.38	2.22	0.10
V15RIGHT	10	1.96	2.30	2.13	0.10
V16LEFT	10	3.34	3.58	3.47	0.07
V16RIGHT	10	2.94	3.64	3.39	0.19
V17LEFT	10	1.06	1.26	1.20	0.07
V17RIGHT	10	0.64	1.37	1.17	0.21
V18LEFT	10	5.42	5.86	5.65	0.13
V18RIGHT	10	5.69	5.94	5.79	0.09
V19LEFT	10	12.04	13.62	12.81	0.55
V19RIGHT	8	12.29	14.32	13.41	0.61
V20LEFT	10	10.17	10.72	10.48	0.18
V20RIGHT	10	9.83	10.84	10.47	0.29
V21LEFT	10	8.18	8.60	8.43	0.17
V21RIGHT	9	7.68	8.72	8.37	0.31

[a] DBA/2J males and females.
[b] Variables described in TABLE III.
[c] Number of individuals measured for each variable.
[d] Minimum, maximum, and standard deviation in mm except for variables 11, 14, 17 and 19, which are in mm^2.

TABLE XV

Descriptive statistics for all variables in the FVB/NJ strain[a]

MALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	10	6.66	7.04	6.77	0.12
V1RIGHT	10	6.62	6.99	6.78	0.13
V2LEFT	10	3.41	3.77	3.60	0.11
V2RIGHT	10	3.25	3.80	3.57	0.15
V3LEFT	10	9.94	10.31	10.19	0.12
V3RIGHT	10	10.03	10.36	10.19	0.14
V4LEFT	10	3.69	4.00	3.83	0.10
V4RIGHT	10	3.72	4.00	3.88	0.08
V5LEFT	10	1.72	1.82	1.76	0.03
V5RIGHT	10	1.76	1.87	1.81	0.04
V7LEFT	10	1.71	1.88	1.82	0.06
V7RIGHT	10	1.69	1.87	1.80	0.06
V11LEFT	10	13.23	14.58	13.76	0.48
V11RIGHT	10	13.06	14.36	13.74	0.42
V14LEFT	10	2.18	2.67	2.42	0.17
V14RIGHT	10	2.22	2.63	2.44	0.15
V15LEFT	10	2.27	2.41	2.34	0.04
V15RIGHT	10	2.20	2.63	2.36	0.11
V16LEFT	10	3.53	3.73	3.60	0.06
V16RIGHT	10	3.44	3.86	3.59	0.11
V17LEFT	10	1.10	1.27	1.17	0.05
V17RIGHT	10	1.10	1.22	1.15	0.04
V18LEFT	10	5.46	5.81	5.65	0.12
V18RIGHT	10	5.33	5.87	5.67	0.18
V19LEFT	10	11.74	13.32	12.57	0.58
V19RIGHT	10	12.40	13.80	13.11	0.52
V20LEFT	10	10.54	10.95	10.77	0.14
V20RIGHT	10	10.49	11.02	10.81	0.18
V21LEFT	10	8.80	8.98	8.89	0.05
V21RIGHT	10	8.66	9.04	8.87	0.12

(continued)

TABLE XV (continued)

Descriptive statistics for all variables in the FVB/NJ strain[a]

FEMALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	10	6.26	8.41	6.74	0.61
V1RIGHT	10	6.43	8.63	6.85	0.64
V2LEFT	10	3.41	4.59	3.69	0.33
V2RIGHT	10	3.43	4.48	3.62	0.31
V3LEFT	10	9.50	12.74	10.23	0.91
V3RIGHT	10	9.73	12.88	10.27	0.93
V4LEFT	10	3.64	4.79	3.89	0.33
V4RIGHT	10	3.75	5.96	4.10	0.66
V5LEFT	10	1.64	2.20	1.76	0.16
V5RIGHT	10	1.74	2.25	1.81	0.16
V7LEFT	10	1.67	2.33	1.86	0.18
V7RIGHT	10	1.69	1.95	1.83	0.09
V11LEFT	10	12.96	23.63	14.40	3.25
V11RIGHT	10	12.85	29.83	14.86	5.27
V14LEFT	10	2.18	4.21	2.55	0.60
V14RIGHT	10	2.20	4.78	2.61	0.77
V15LEFT	10	2.20	2.91	2.40	0.21
V15RIGHT	10	2.25	5.30	2.60	0.95
V16LEFT	10	3.50	4.55	3.64	0.32
V16RIGHT	10	3.46	6.81	3.85	1.04
V17LEFT	10	1.04	2.18	1.24	0.33
V17RIGHT	10	1.12	2.09	1.23	0.30
V18LEFT	10	5.27	7.17	5.70	0.53
V18RIGHT	10	5.48	5.76	5.66	0.09
V19LEFT	10	11.40	21.17	12.97	2.93
V19RIGHT	10	12.46	18.35	13.51	1.73
V20LEFT	10	10.38	13.62	10.93	0.96
V20RIGHT	10	10.49	13.65	11.02	0.93
V21LEFT	10	8.45	11.03	8.93	0.75
V21RIGHT	10	8.51	12.12	9.04	1.09

[a] FVB/NJ males and females.
[b] Variables described in TABLE III.
[c] Number of individuals measured for each variable.
[d] Minimum, maximum, and standard deviation in mm except for variables 11, 14, 17 and 19, which are in mm^2.

TABLE XVI

Descriptive statistics for all variables in the MOLF/Ei strain[a]

MALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	10	5.38	5.90	5.65	0.18
V1RIGHT	10	5.46	6.10	5.77	0.22
V2LEFT	10	2.99	3.49	3.30	0.18
V2RIGHT	10	3.09	3.43	3.24	0.12
V3LEFT	10	8.45	9.14	8.79	0.19
V3RIGHT	10	8.38	9.12	8.84	0.21
V4LEFT	10	3.74	4.08	3.90	0.12
V4RIGHT	10	3.62	4.08	3.88	0.12
V5LEFT	10	1.67	1.84	1.75	0.05
V5RIGHT	10	1.71	1.81	1.75	0.03
V7LEFT	10	1.55	1.72	1.63	0.06
V7RIGHT	10	1.44	1.71	1.58	0.07
V11LEFT	10	10.70	12.36	11.26	0.46
V11RIGHT	10	10.82	11.59	11.30	0.24
V14LEFT	10	0.81	1.23	1.07	0.13
V14RIGHT	10	0.81	1.22	1.05	0.13
V15LEFT	10	1.78	2.06	1.92	0.10
V15RIGHT	10	1.88	2.16	2.05	0.08
V16LEFT	10	3.05	3.32	3.16	0.09
V16RIGHT	10	3.08	3.33	3.20	0.08
V17LEFT	10	0.72	0.89	0.79	0.04
V17RIGHT	10	0.68	0.85	0.76	0.06
V18LEFT	10	5.16	5.59	5.34	0.14
V18RIGHT	10	5.10	5.46	5.30	0.12
V19LEFT	10	10.24	12.12	11.22	0.56
V19RIGHT	10	10.31	11.86	11.28	0.44
V20LEFT	10	9.06	9.82	9.44	0.19
V20RIGHT	10	9.21	9.75	9.53	0.18
V21LEFT	10	7.95	8.43	8.11	0.16
V21RIGHT	10	7.89	8.35	8.17	0.15

(continued)

TABLE XVI (continued)

Descriptive statistics for all variables in the MOLF/Ei strain[a]

FEMALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	10	5.42	6.21	5.77	0.22
V1RIGHT	10	5.30	6.17	5.74	0.25
V2LEFT	10	3.05	3.61	3.34	0.14
V2RIGHT	10	3.04	3.60	3.28	0.18
V3LEFT	10	8.72	9.06	8.92	0.11
V3RIGHT	10	8.38	9.05	8.84	0.19
V4LEFT	10	3.84	4.19	4.03	0.12
V4RIGHT	10	3.87	4.27	4.12	0.14
V5LEFT	10	1.65	1.88	1.76	0.08
V5RIGHT	10	1.73	1.86	1.80	0.04
V7LEFT	10	1.55	1.80	1.67	0.08
V7RIGHT	10	1.58	1.77	1.66	0.06
V11LEFT	10	10.99	11.77	11.42	0.26
V11RIGHT	10	10.20	11.85	11.24	0.43
V14LEFT	10	0.92	1.19	1.09	0.09
V14RIGHT	10	0.89	1.10	0.99	0.08
V15LEFT	10	1.88	2.11	1.99	0.08
V15RIGHT	10	1.80	2.11	2.02	0.08
V16LEFT	10	3.15	3.37	3.22	0.06
V16RIGHT	10	3.07	3.33	3.25	0.08
V17LEFT	10	0.75	0.84	0.80	0.03
V17RIGHT	10	0.69	0.87	0.75	0.05
V18LEFT	10	5.23	5.62	5.44	0.14
V18RIGHT	10	5.18	5.66	5.42	0.13
V19LEFT	10	10.95	12.48	11.86	0.47
V19RIGHT	10	11.07	12.72	12.18	0.53
V20LEFT	10	9.44	9.83	9.66	0.11
V20RIGHT	10	9.12	9.77	9.62	0.19
V21LEFT	10	8.17	8.37	8.28	0.07
V21RIGHT	10	7.81	8.47	8.24	0.19

[a] MOLF/Ei males and females.
[b] Variables described in TABLE III.
[c] Number of individuals measured for each variable.
[d] Minimum, maximum, and standard deviation in mm except for variables 11, 14, 17 and 19, which are in mm^2.

TABLE XVII

Descriptive statistics for all variables in the PERA/Ei strain[a]

MALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	10	6.45	7.21	6.84	0.30
V1RIGHT	8	6.47	7.24	6.75	0.27
V2LEFT	10	3.18	3.90	3.43	0.26
V2RIGHT	10	2.69	3.84	3.37	0.31
V3LEFT	10	9.95	10.35	10.14	0.13
V3RIGHT	8	9.89	10.31	10.09	0.17
V4LEFT	10	3.80	4.00	3.89	0.07
V4RIGHT	9	3.96	4.17	4.08	0.08
V5LEFT	10	1.63	1.78	1.70	0.04
V5RIGHT	10	1.52	1.82	1.72	0.09
V7LEFT	10	1.83	2.10	1.96	0.09
V7RIGHT	9	1.91	2.06	1.98	0.05
V11LEFT	10	12.34	13.59	13.18	0.38
V11RIGHT	10	12.35	13.40	12.84	0.38
V14LEFT	10	1.99	2.46	2.10	0.13
V14RIGHT	8	1.89	2.24	2.08	0.11
V15LEFT	10	2.14	2.35	2.23	0.08
V15RIGHT	10	2.14	2.60	2.30	0.13
V16LEFT	10	3.26	3.55	3.40	0.12
V16RIGHT	10	3.27	3.87	3.43	0.19
V17LEFT	10	1.04	1.30	1.17	0.07
V17RIGHT	10	1.04	1.23	1.12	0.06
V18LEFT	10	5.64	5.88	5.78	0.09
V18RIGHT	9	5.59	5.95	5.78	0.11
V19LEFT	10	11.63	12.77	12.17	0.36
V19RIGHT	9	12.66	13.70	13.00	0.34
V20LEFT	10	10.43	10.81	10.63	0.12
V20RIGHT	9	10.38	10.84	10.61	0.15
V21LEFT	10	8.65	9.02	8.82	0.12
V21RIGHT	9	8.60	8.99	8.76	0.14

(continued)

TABLE XVII (continued)

Descriptive statistics for all variables in the PERA/Ei strain[a]

FEMALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	10	6.14	7.06	6.71	0.30
V1RIGHT	10	6.32	7.08	6.69	0.32
V2LEFT	10	2.92	3.78	3.37	0.29
V2RIGHT	10	2.94	3.82	3.33	0.30
V3LEFT	10	9.64	10.09	9.94	0.19
V3RIGHT	10	9.64	10.11	9.88	0.16
V4LEFT	10	3.71	4.05	3.92	0.12
V4RIGHT	10	3.86	4.23	4.02	0.13
V5LEFT	10	1.65	1.75	1.70	0.03
V5RIGHT	10	1.65	1.95	1.77	0.09
V7LEFT	10	1.89	2.11	2.02	0.06
V7RIGHT	10	1.90	2.17	2.02	0.10
V11LEFT	10	12.06	13.65	12.84	0.46
V11RIGHT	10	11.78	13.40	12.66	0.45
V14LEFT	10	1.75	2.11	1.95	0.12
V14RIGHT	10	1.76	2.08	1.90	0.10
V15LEFT	10	2.15	2.32	2.23	0.06
V15RIGHT	10	2.18	2.36	2.26	0.06
V16LEFT	10	3.10	3.50	3.36	0.13
V16RIGHT	10	3.25	3.62	3.38	0.15
V17LEFT	10	1.02	1.20	1.07	0.06
V17RIGHT	10	0.91	1.19	1.04	0.10
V18LEFT	10	5.41	5.86	5.71	0.14
V18RIGHT	10	5.53	5.94	5.74	0.14
V19LEFT	10	11.14	13.51	12.28	0.65
V19RIGHT	10	11.29	13.53	12.61	0.73
V20LEFT	10	10.19	10.72	10.50	0.20
V20RIGHT	10	10.17	10.79	10.53	0.19
V21LEFT	10	8.38	8.91	8.66	0.18
V21RIGHT	10	8.39	8.76	8.63	0.13

[a] PERA/Ei males and females.
[b] Variables described in TABLE III.
[c] Number of individuals measured for each variable.
[d] Minimum, maximum, and standard deviation in mm except for variables 11, 14, 17 and 19, which are in mm^2.

TABLE XVIII

Descriptive statistics for all variables in the SJL/J strain[a]

MALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	10	6.60	6.96	6.77	0.11
V1RIGHT	9	6.20	7.18	6.76	0.27
V2LEFT	10	3.23	3.95	3.68	0.19
V2RIGHT	10	3.41	3.83	3.66	0.12
V3LEFT	10	9.69	10.47	10.30	0.23
V3RIGHT	9	9.52	10.78	10.30	0.33
V4LEFT	10	4.04	4.36	4.18	0.10
V4RIGHT	10	4.25	4.80	4.49	0.19
V5LEFT	10	1.71	1.90	1.76	0.05
V5RIGHT	10	1.73	1.90	1.82	0.05
V7LEFT	10	1.59	1.83	1.70	0.07
V7RIGHT	10	1.65	1.94	1.73	0.08
V11LEFT	10	12.24	13.51	12.72	0.39
V11RIGHT	10	11.35	12.72	12.12	0.46
V14LEFT	10	2.35	2.69	2.51	0.11
V14RIGHT	9	2.35	2.87	2.54	0.17
V15LEFT	10	1.96	2.23	2.09	0.08
V15RIGHT	10	1.99	2.17	2.10	0.06
V16LEFT	10	3.21	3.35	3.26	0.05
V16RIGHT	10	3.10	3.32	3.22	0.08
V17LEFT	10	1.01	1.16	1.06	0.05
V17RIGHT	10	0.92	1.09	1.02	0.05
V18LEFT	10	5.64	6.22	5.99	0.15
V18RIGHT	10	5.77	6.32	6.08	0.17
V19LEFT	10	12.26	14.45	13.35	0.53
V19RIGHT	10	13.02	15.62	14.43	0.69
V20LEFT	10	10.37	10.98	10.83	0.18
V20RIGHT	10	10.48	11.16	10.88	0.18
V21LEFT	10	8.45	9.02	8.88	0.17
V21RIGHT	10	8.34	9.15	8.87	0.21

(continued)

TABLE XVIII (continued)

Descriptive statistics for all variables in the SJL/J strain[a]

FEMALES[b]	N[c]	Minimum[d]	Maximum[d]	Mean[d]	Std. Deviation[d]
V1LEFT	9	6.18	6.76	6.52	0.19
V1RIGHT	10	6.31	6.73	6.52	0.15
V2LEFT	10	3.45	3.80	3.61	0.11
V2RIGHT	10	3.28	3.77	3.55	0.16
V3LEFT	9	9.71	10.27	9.98	0.21
V3RIGHT	10	9.57	10.20	9.92	0.25
V4LEFT	9	4.03	4.36	4.19	0.11
V4RIGHT	10	3.92	4.82	4.39	0.24
V5LEFT	10	1.66	1.84	1.76	0.05
V5RIGHT	10	1.67	1.88	1.79	0.06
V7LEFT	10	1.70	2.05	1.84	0.12
V7RIGHT	10	1.65	2.03	1.81	0.11
V11LEFT	10	11.66	13.16	12.40	0.52
V11RIGHT	10	10.89	12.63	11.69	0.49
V14LEFT	9	2.07	2.50	2.30	0.14
V14RIGHT	10	2.13	2.54	2.32	0.13
V15LEFT	10	1.93	2.08	2.01	0.06
V15RIGHT	10	1.96	2.16	2.04	0.06
V16LEFT	10	3.08	3.28	3.22	0.06
V16RIGHT	10	3.06	3.33	3.20	0.08
V17LEFT	10	0.93	1.13	1.03	0.06
V17RIGHT	10	0.93	1.11	0.98	0.07
V18LEFT	10	5.76	6.16	5.98	0.16
V18RIGHT	10	5.65	6.24	5.96	0.18
V19LEFT	9	12.55	13.83	13.21	0.39
V19RIGHT	10	12.94	15.65	14.00	0.84
V20LEFT	10	10.34	10.96	10.68	0.21
V20RIGHT	10	10.35	11.01	10.66	0.22
V21LEFT	10	8.42	8.91	8.68	0.20
V21RIGHT	10	8.31	8.92	8.63	0.22

[a] SJL/J males and females.
[b] Variables described in TABLE III.
[c] Number of individuals measured for each variable.
[d] Minimum, maximum, and standard deviation in mm except for variables 11, 14, 17 and 19, which are in mm^2.

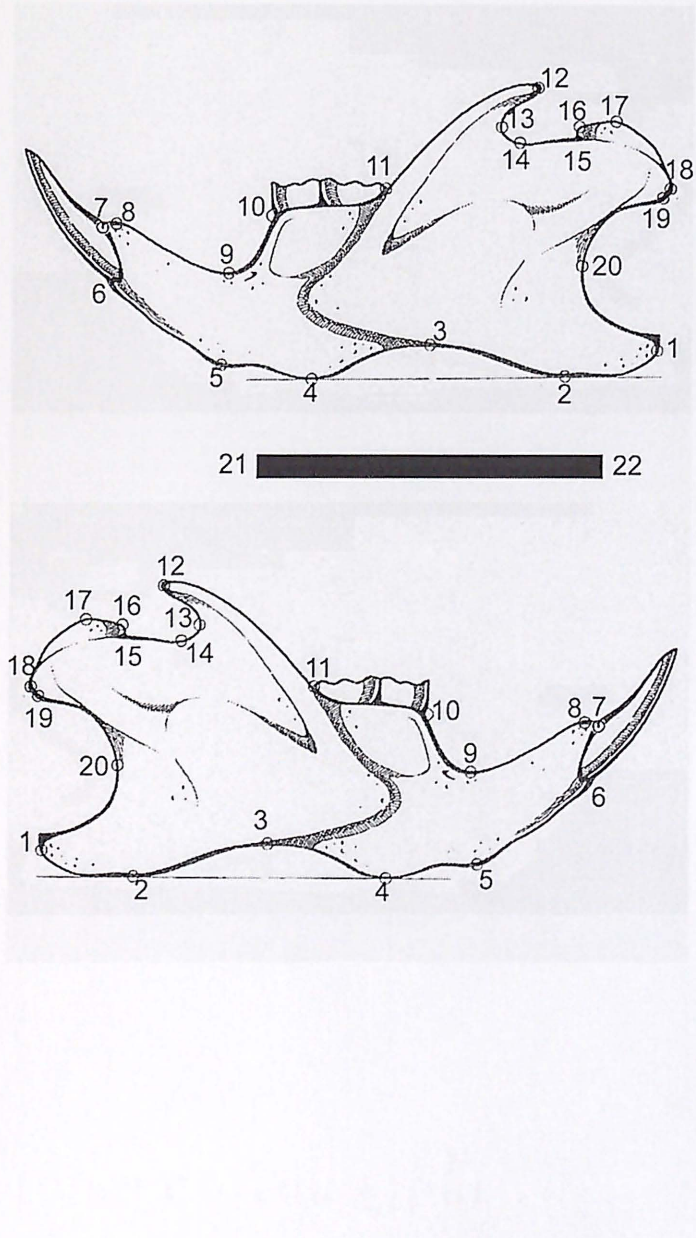


FIGURE 1. Collection of landmarks used to calculate hemi-mandible variables. Landmarks were viewed from the buccal side and digitized to determine the Cartesian coordinates for each. Landmarks were digitized in numeric order. The last two landmarks (21 and 22) were used to measure the size bar, which is used to calculate actual distances in mm. Landmarks adapted from those used by Atchley et al. [33] Upper = left side, and Lower = right side.

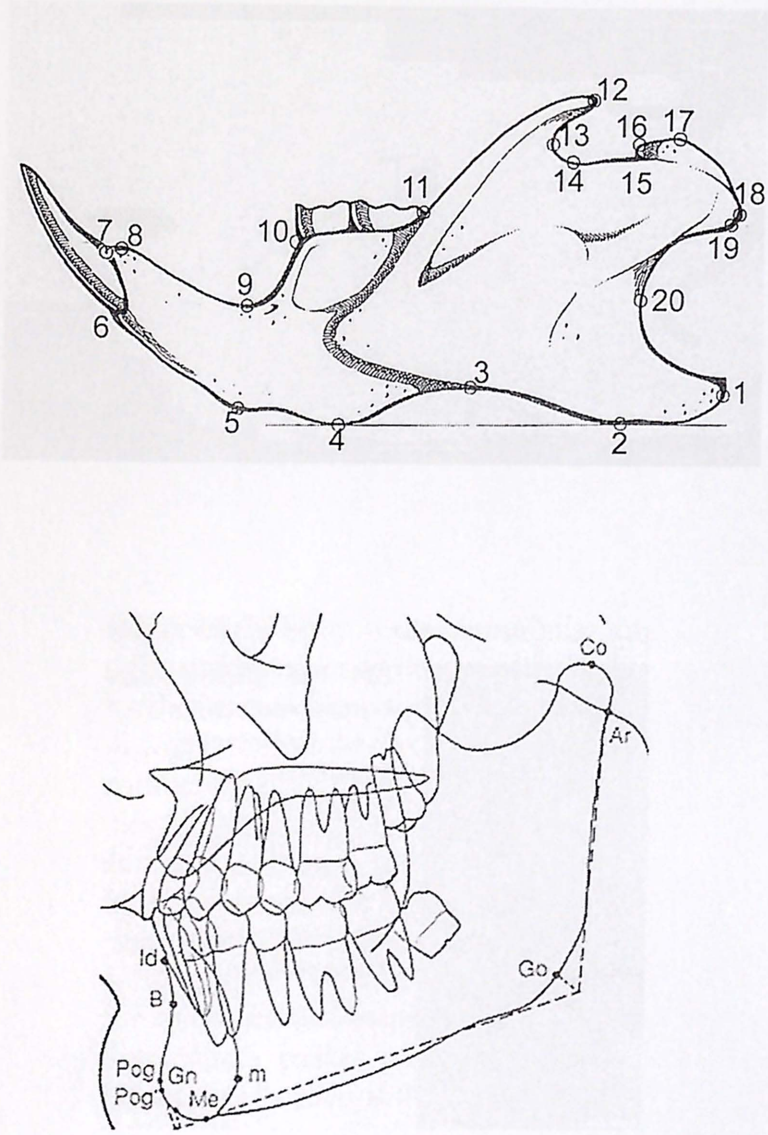


FIGURE 2. Mouse and human mandibles. Upper panel is the buccal view of the left hemi-mandible with landmarks 1 – 20 indicated (see TABLE II for descriptions). Adapted from Atchley, et al.[33] Lower panel is a human cephalometric tracing adapted from Athanasiou.[36]

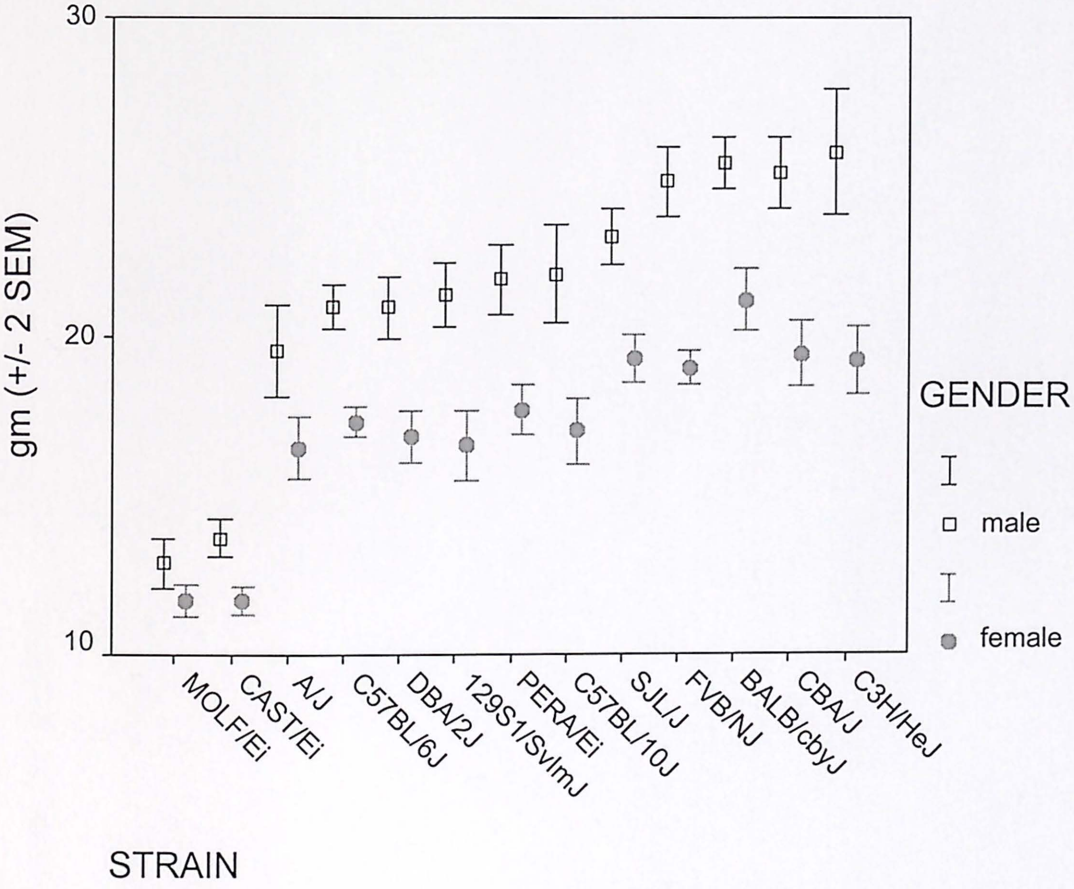


FIGURE 3. Body weights. Mean body weights in grams $\pm$ 2SEM. Males = open squares, and females = solid circles.

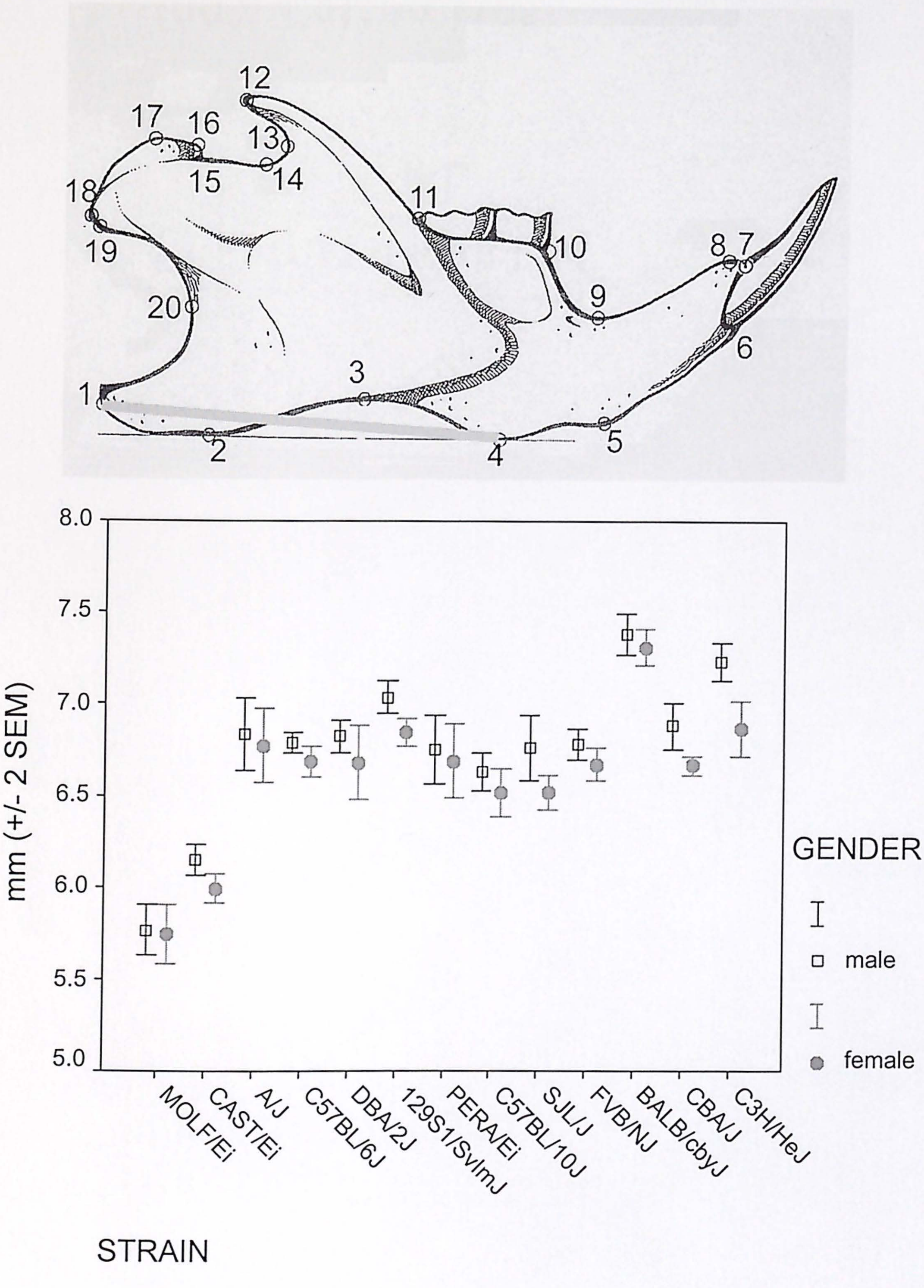
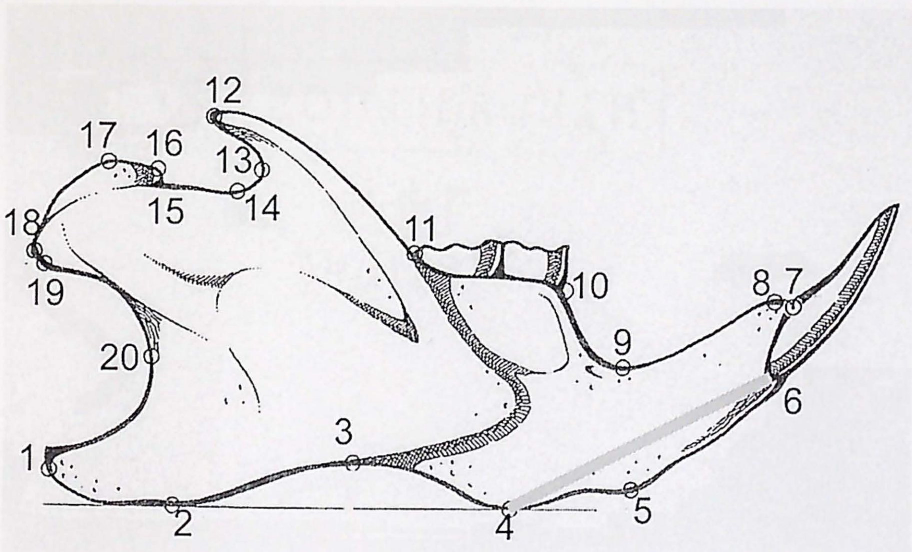


FIGURE 4. Variable 1 Right, Posterior Mandible Length. Upper panel shows buccal view of the right hemi-mandible. Landmarks 1 and 4 determine variable 1. Lower panel shows the lengths of variable 1 in mm (±2 SEM) across all strains measured. Strains are arranged according to increasing body weight (FIGURE 3). Males = open squares, and females = solid circles.



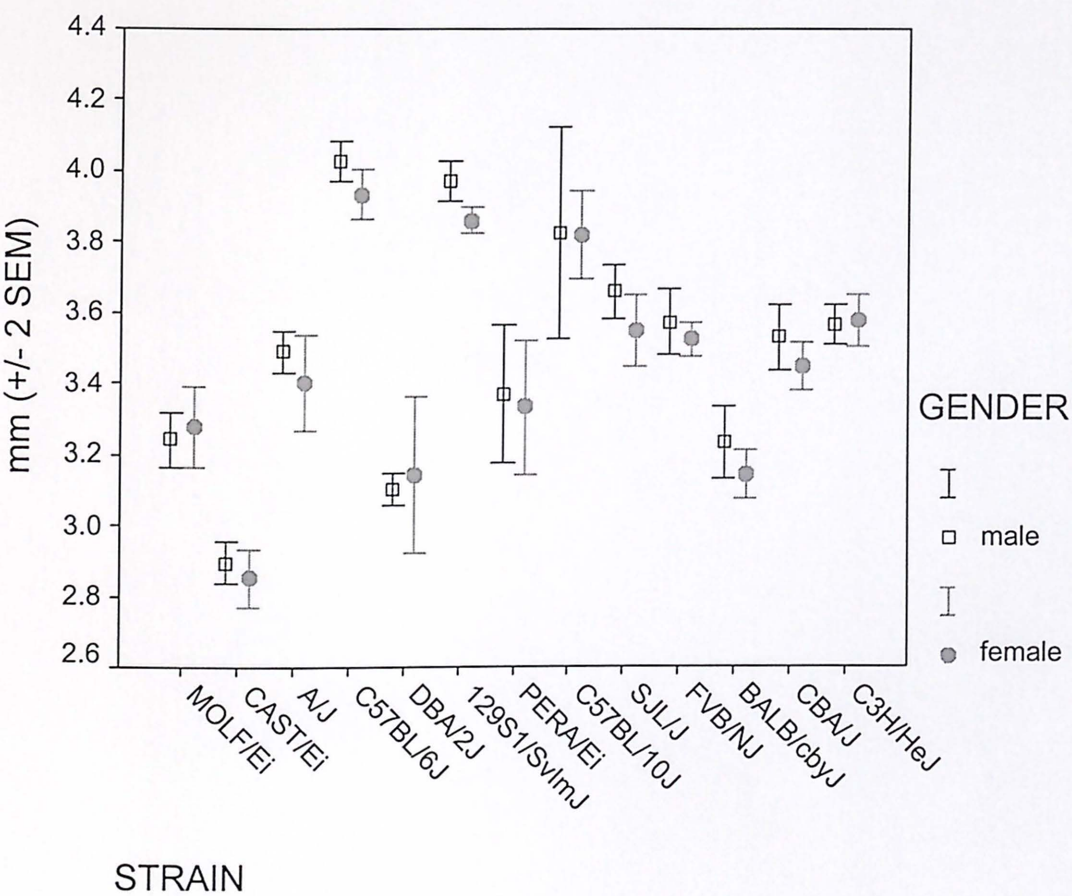
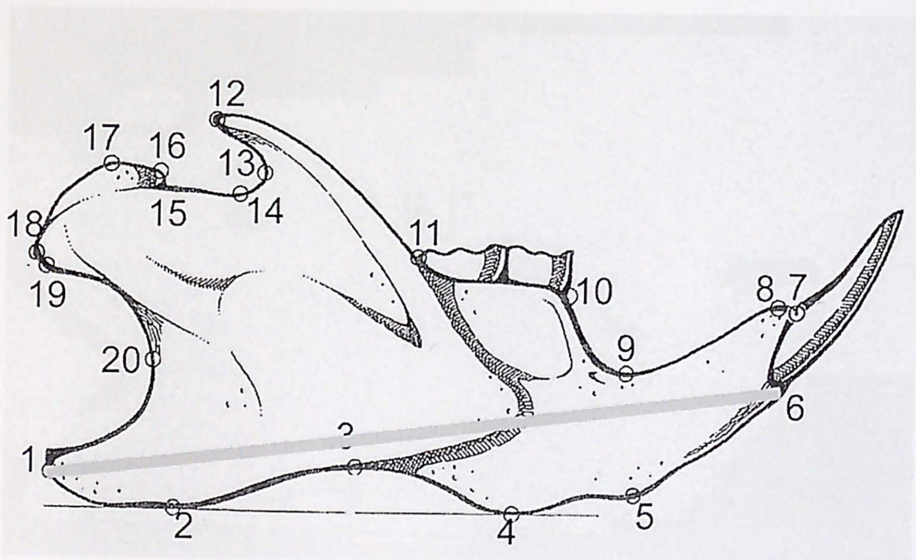


FIGURE 5. Variable 2 Right, Anterior Mandible Length. Upper panel shows buccal view of the right hemi-mandible. Landmarks 4 and 6 determined variable 2. Lower panel shows the length of variable 2 in mm (±2 SEM). Strains are arranged according to body weight (FIGURE 3). Males = open squares, and females = solid circles.



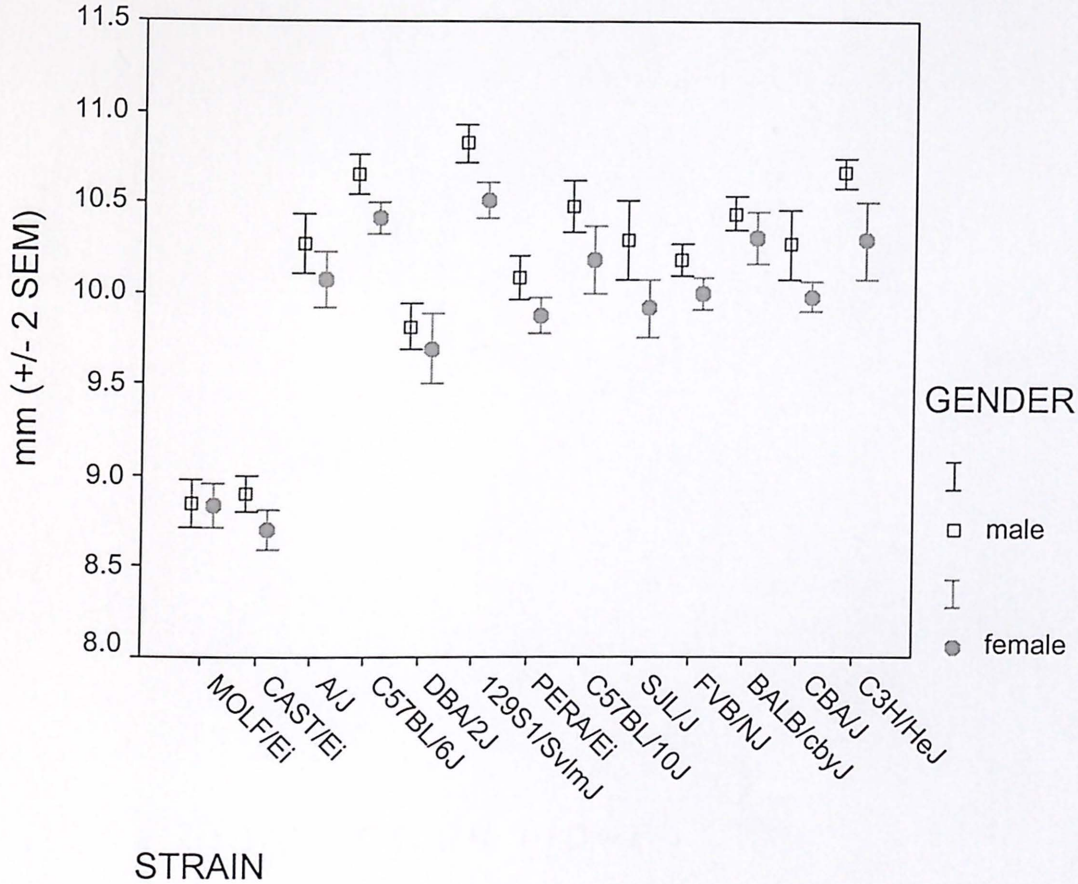


FIGURE 6. Variable 3 Right, Total Mandibular Length. Upper panel shows buccal view of the right hemi-mandible. Landmarks 1 and 6 determined variable 3. Lower panel shows the length of variable 3 in mm (± 2 SEM). Strains are arranged according to body weight (FIGURE 3). Males = open squares, and females = solid circles.

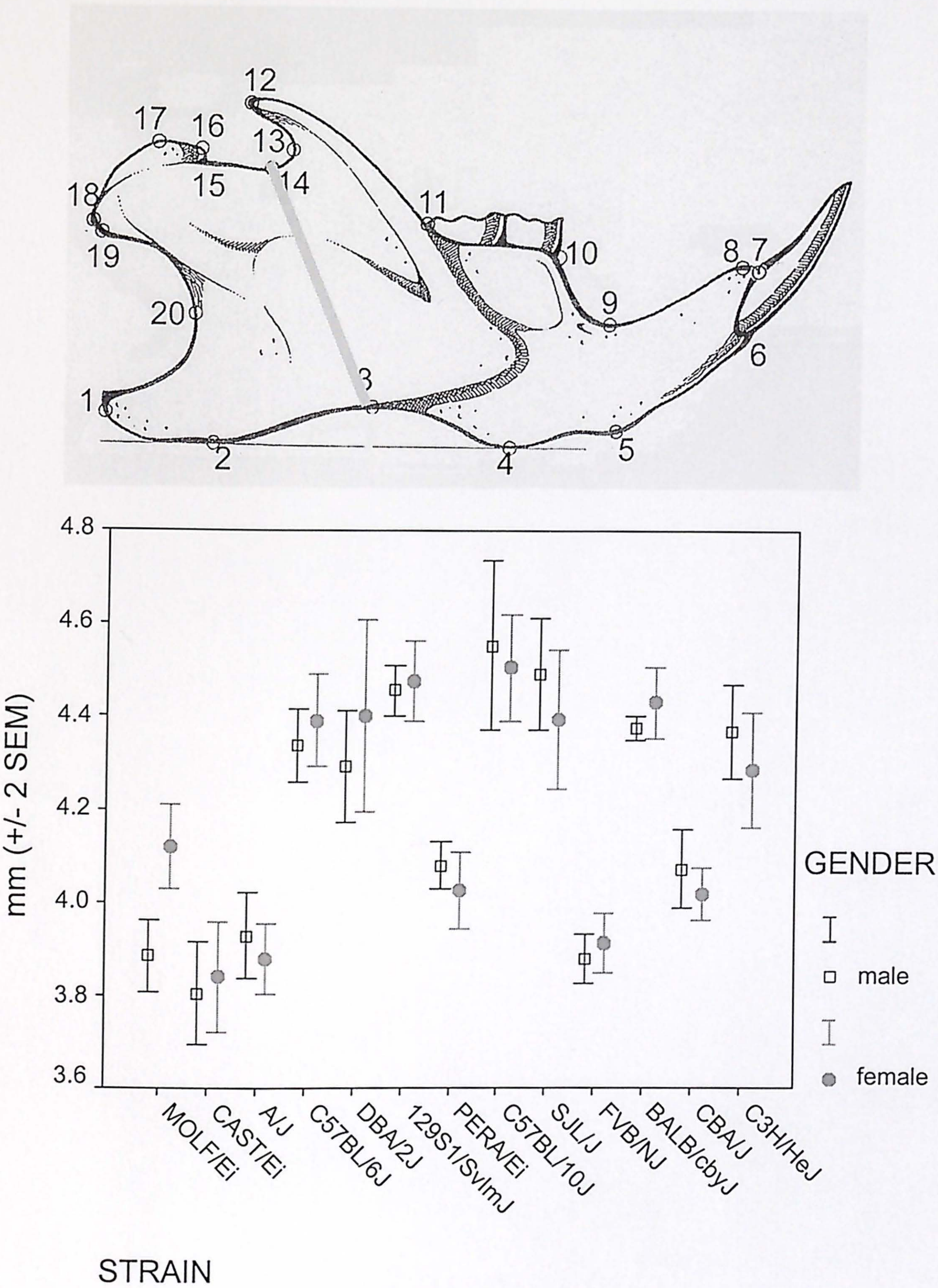


FIGURE 7. Variable 4 Right, Height of Ramus. Upper panel shows buccal view of the right hemi-mandible. Landmarks 3 and 14 determined variable 4. Lower panel shows the length of variable 4 in mm (±2 SEM). Strains are arranged according to body weight (FIGURE 3). Males = open squares, and females = solid circles.

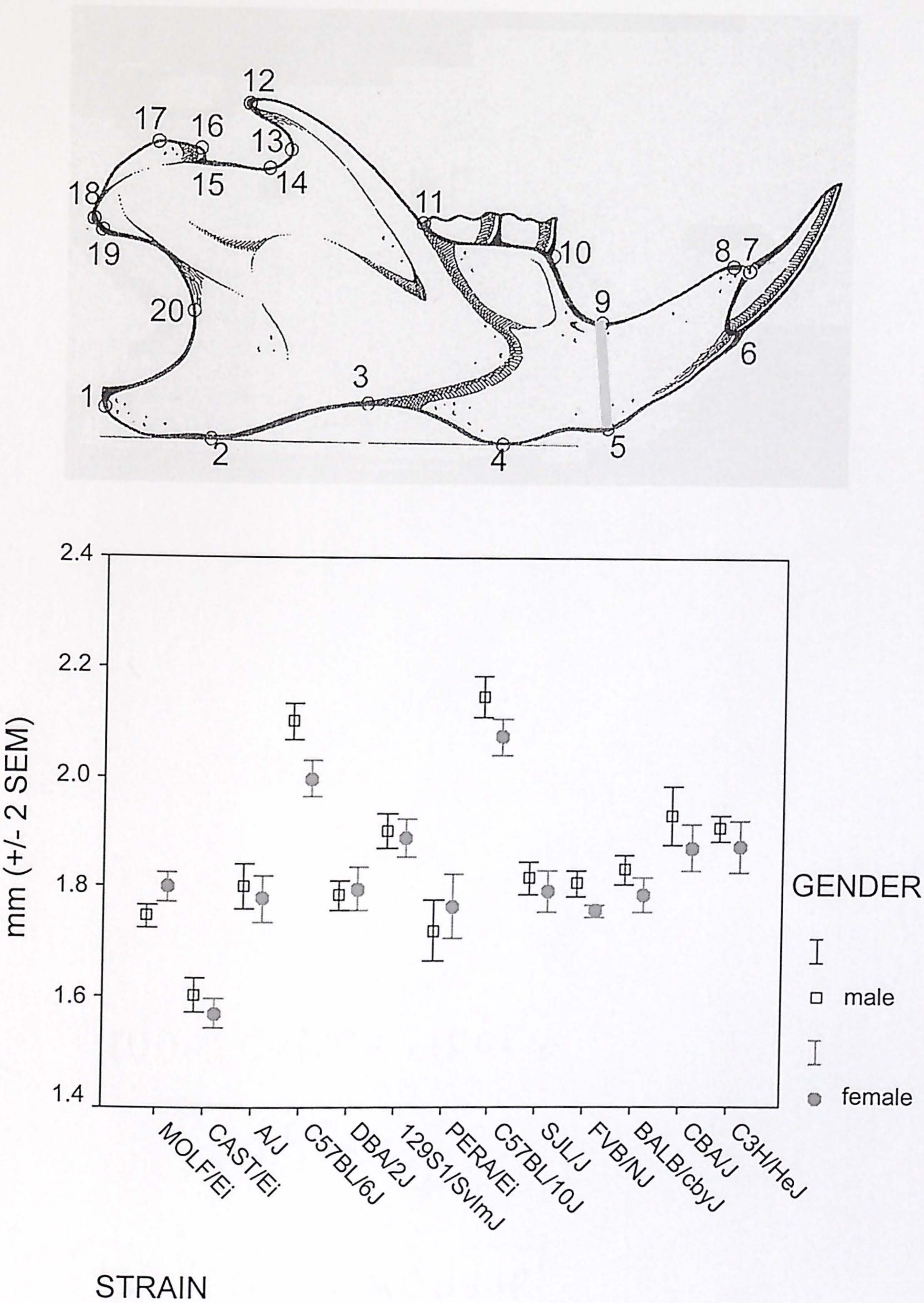
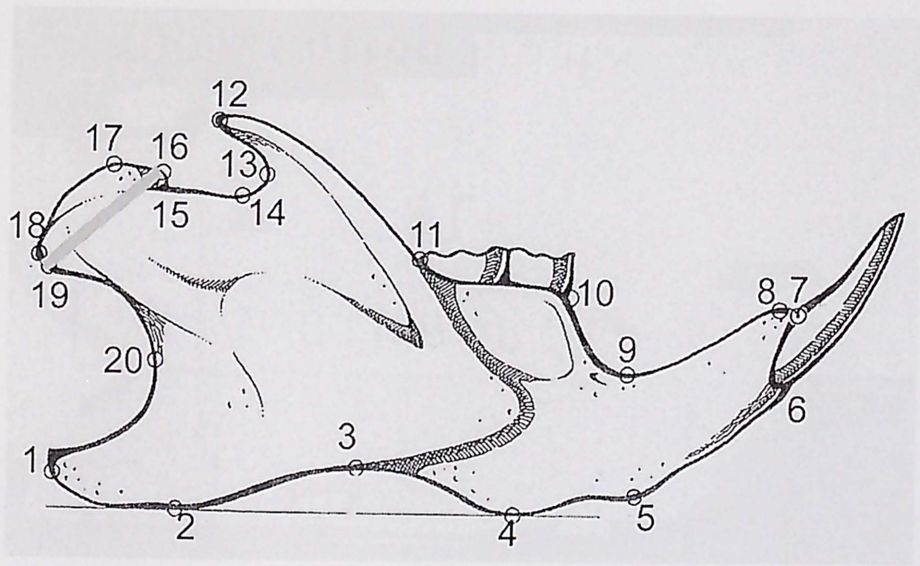


FIGURE 8. Variable 5 Right, Height at Incisor region. Upper panel shows buccal view of the right hemi-mandible. Landmarks 5 and 9 determined variable 5. Lower panel shows the length of variable 5 in mm ($\pm$2 SEM). Strains are arranged according to body weight (FIGURE 3). Males = open squares, and females = solid circles.



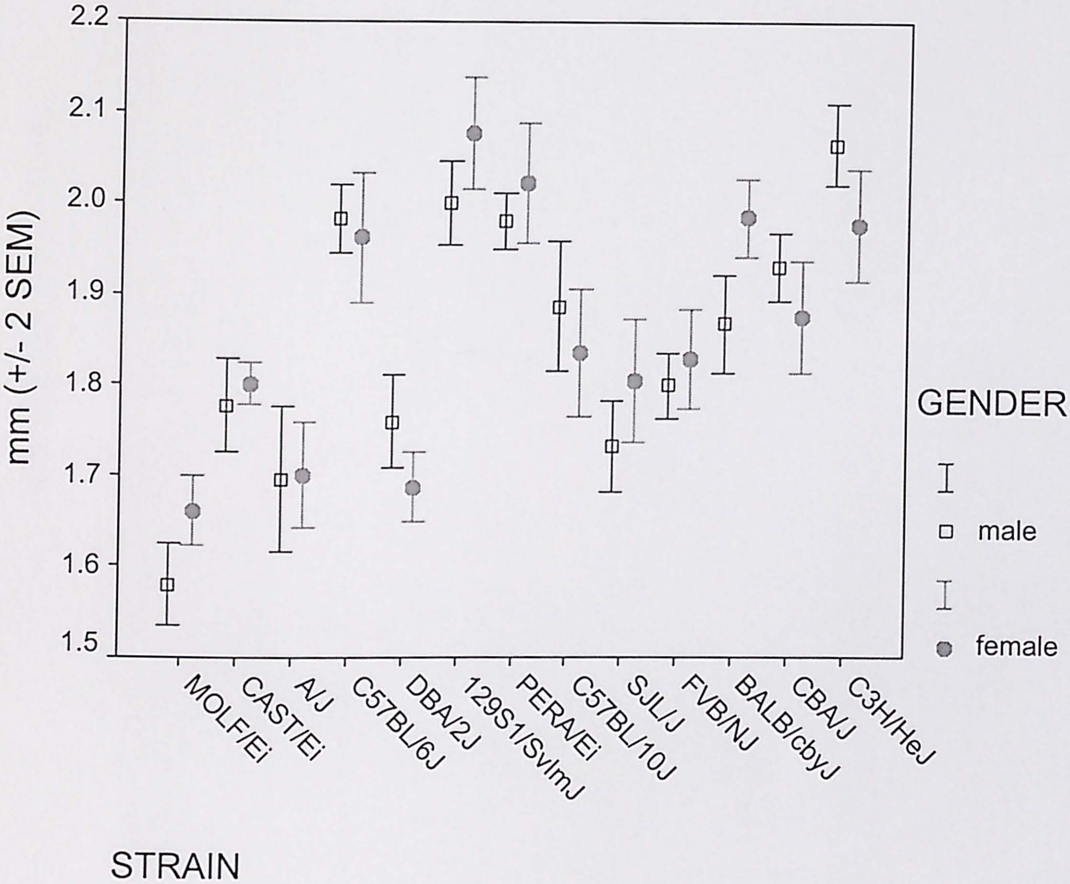
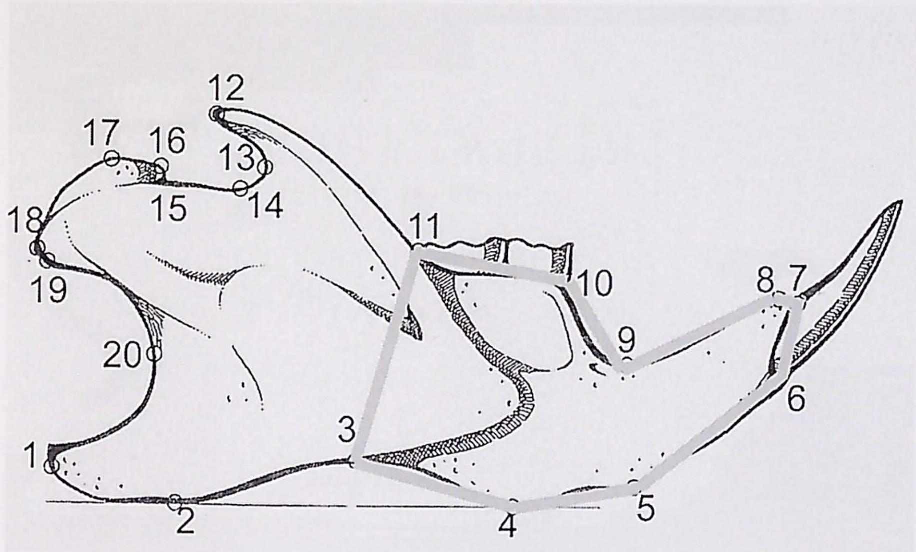


FIGURE 9. Variable 7 Right, Condyloid Width. Upper panel shows buccal view of the right hemi-mandible. Landmarks 16 and 19 determined variable 7. Lower panel shows the length of variable 7 in mm (±2 SEM). Strains are arranged according to body weight (FIGURE 3). Males = open squares, and females = solid circles.



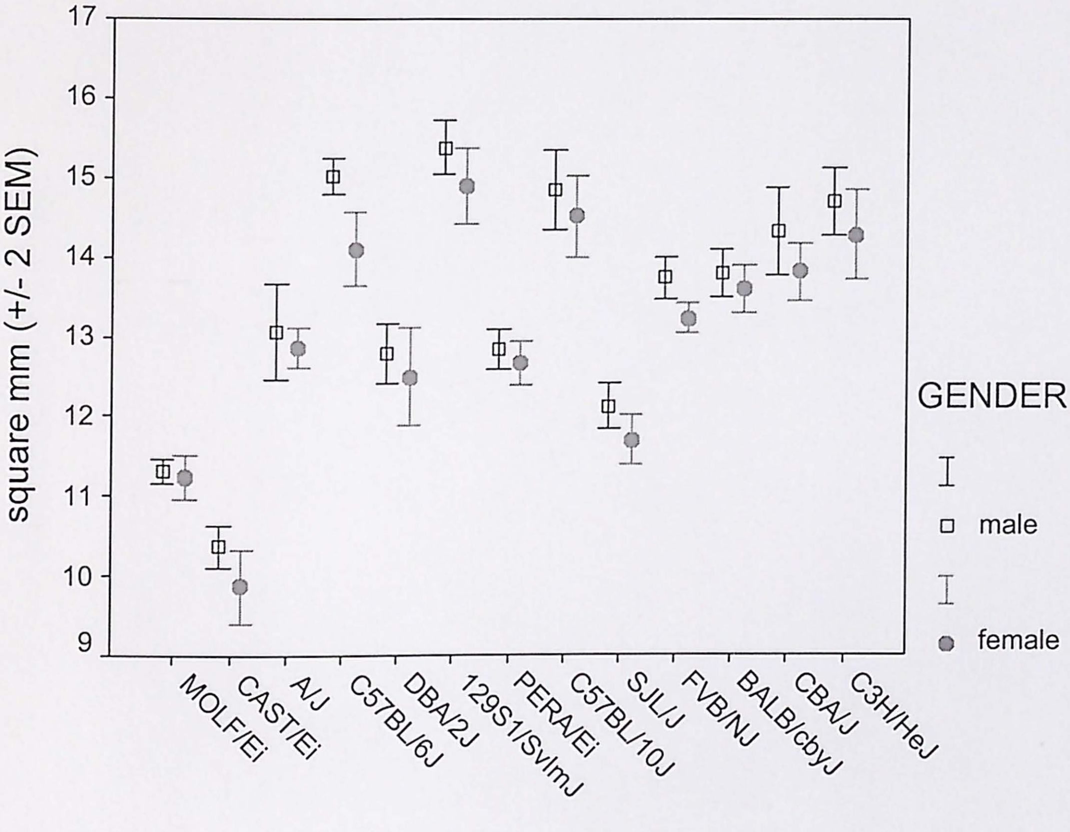
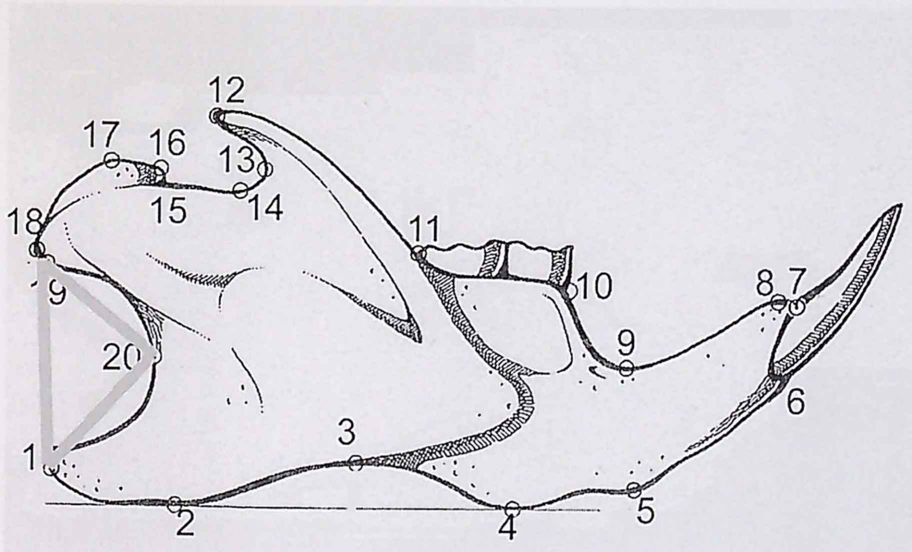


FIGURE 10. Variable 11 Right, Area of Anterior Mandible. Upper panel shows buccal view of the right hemi-mandible. Landmarks 3, 4, 5, 6, 7, 8, 9, 10 and 11 determined variable 11. Lower panel shows the area of variable 11 in mm^2 ($\pm$2 SEM). Strains are arranged according to body weight (FIGURE 3). Males = open squares, and females = solid circles.



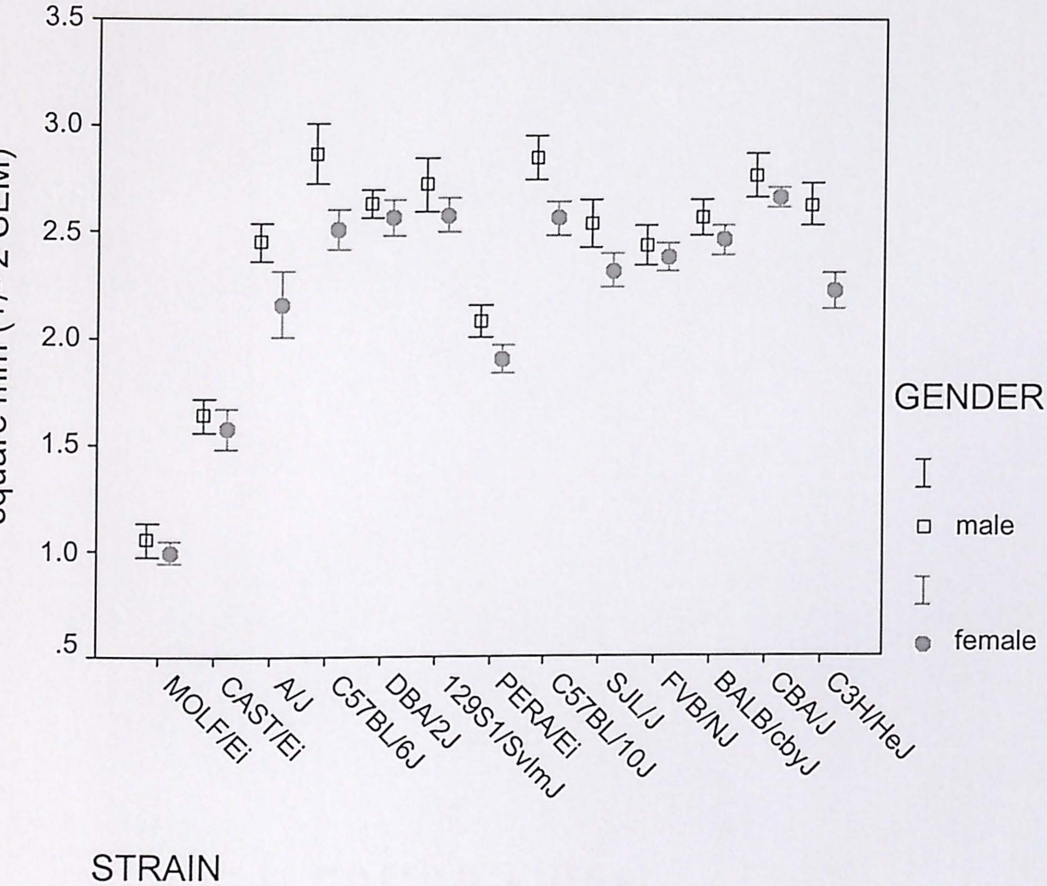


FIGURE 11. Variable 14 Right, Area between Angular and Condyloid Process. Upper panel shows buccal view of the right hemi-mandible. Landmarks 1, 19 and 20 determined variable 14. Lower panel shows the area of variable 14 in mm^2 ($\pm$2 SEM). Strains are arranged according to body weight (FIGURE 3). Males = open squares, and females = solid circle.

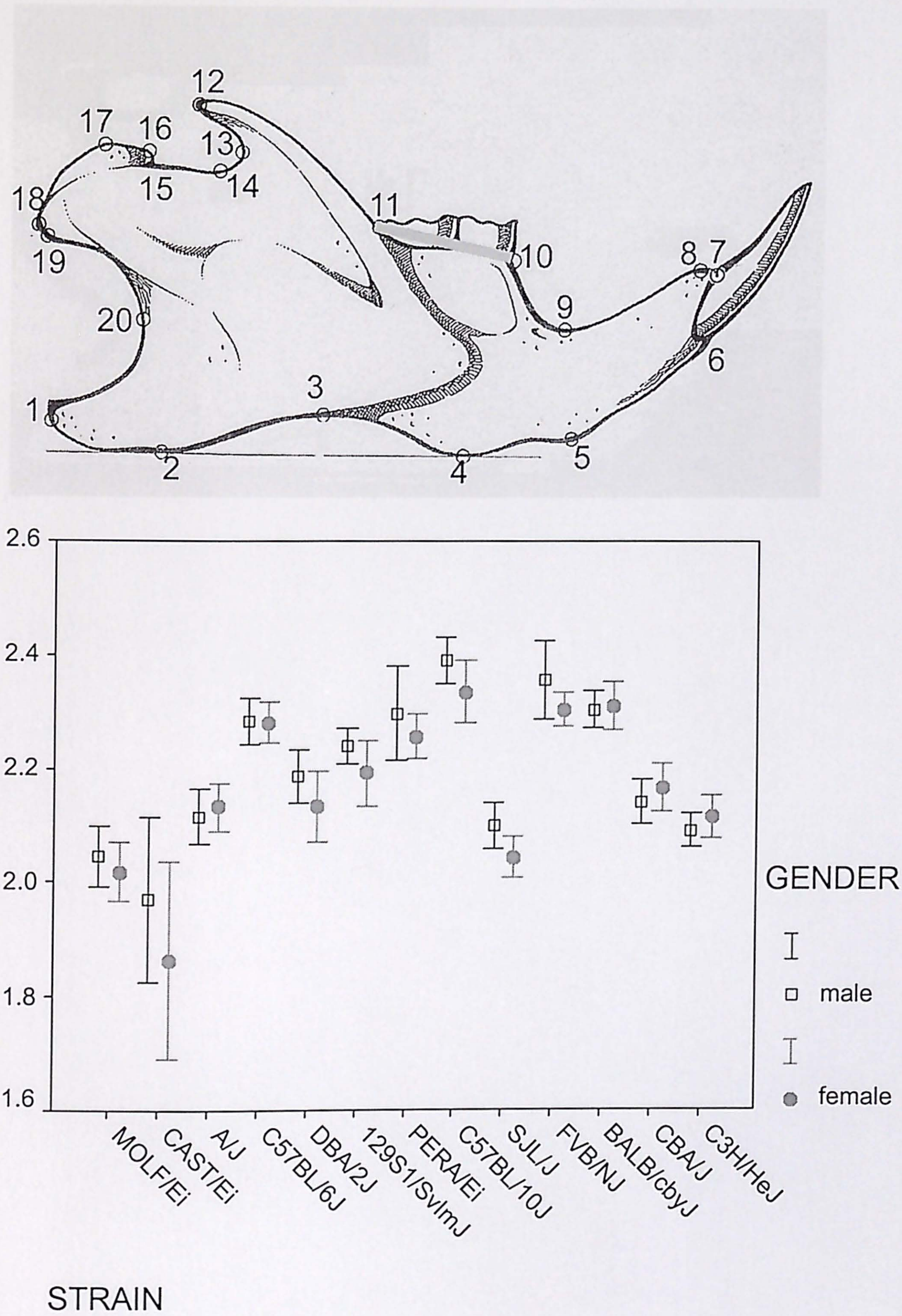


FIGURE 12. Variable 15 Right, Arch Length of Posterior Teeth. Upper panel shows buccal view of the right hemi-mandible. Landmarks 10 and 11 determined variable 15. Lower panel shows the length of variable 15 in mm (±2 SEM). Strains are arranged according to body weight (FIGURE 3). Males = open squares, and females = solid circles.

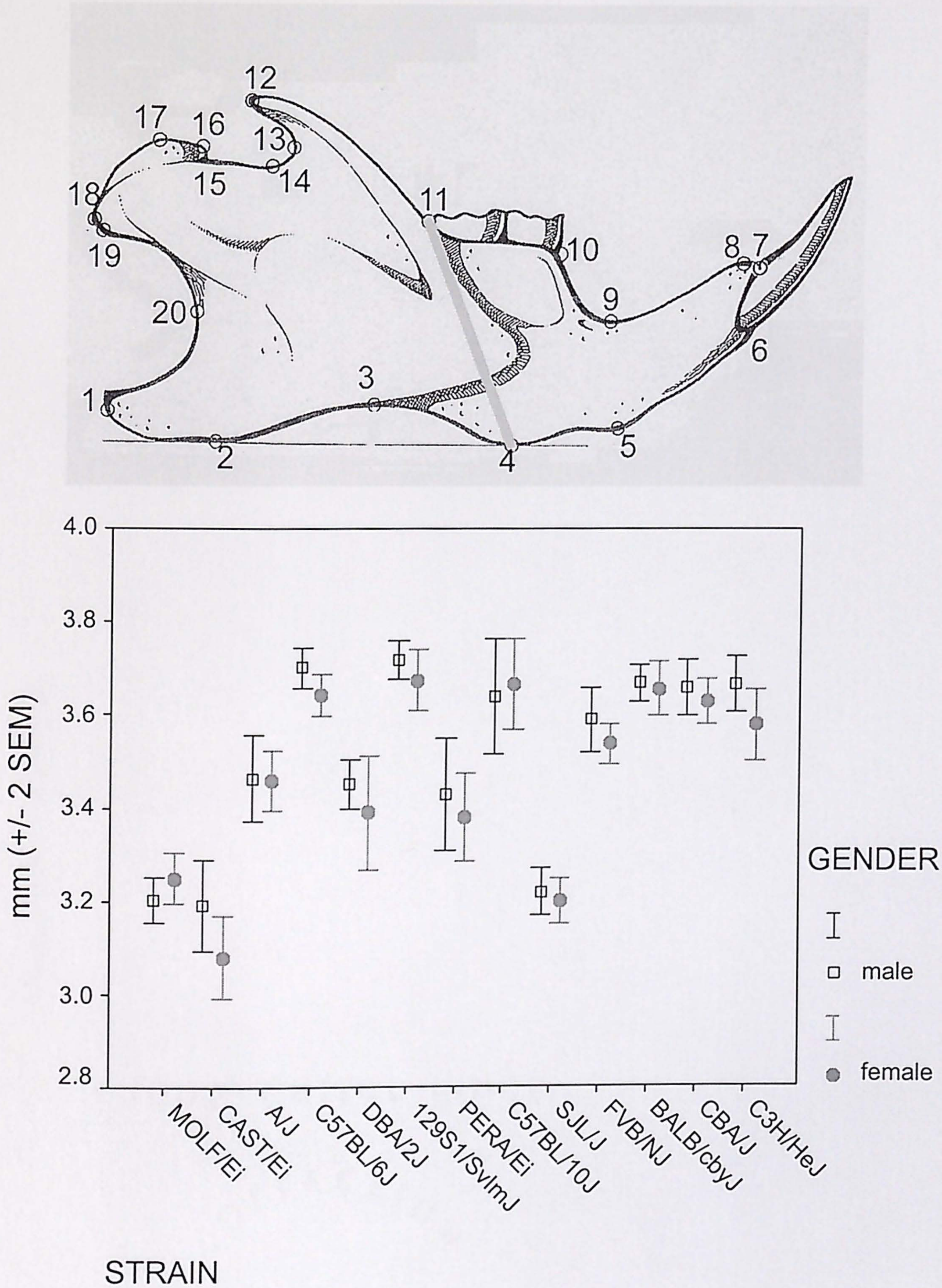


FIGURE 13. Variable 16 Right, Height of Posterior Area of Anterior Mandible. Upper panel shows buccal view of the right hemi-mandible. Landmarks 4 and 11 determined variable 15. Lower panel shows the length of variable 15 in mm (±2 SEM). Strains are arranged according to body weight (FIGURE 3). Males = open squares, and females = solid circles.

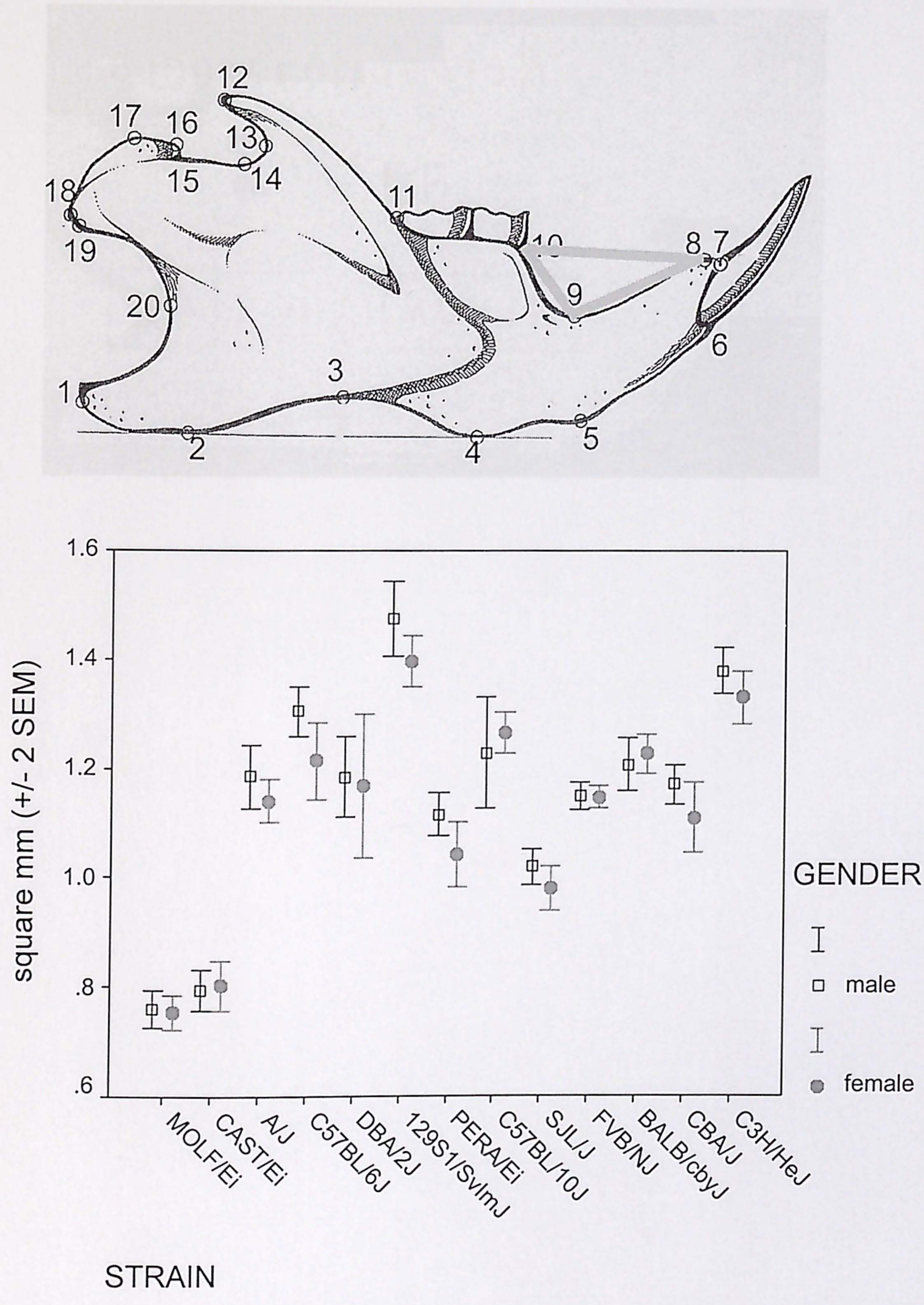


FIGURE 14. Variable 17 Right, Concavity of Incisor Area to most Anterior Molar. Upper panel shows buccal view of the right hemi-mandible. Landmarks 8,9 and 10 determined variable 17. Lower panel shows the area of variable 17 in mm^2 ($\pm$2 SEM). Strains are arranged according to body weight (FIGURE 3). Males = open squares, and females = solid circles.

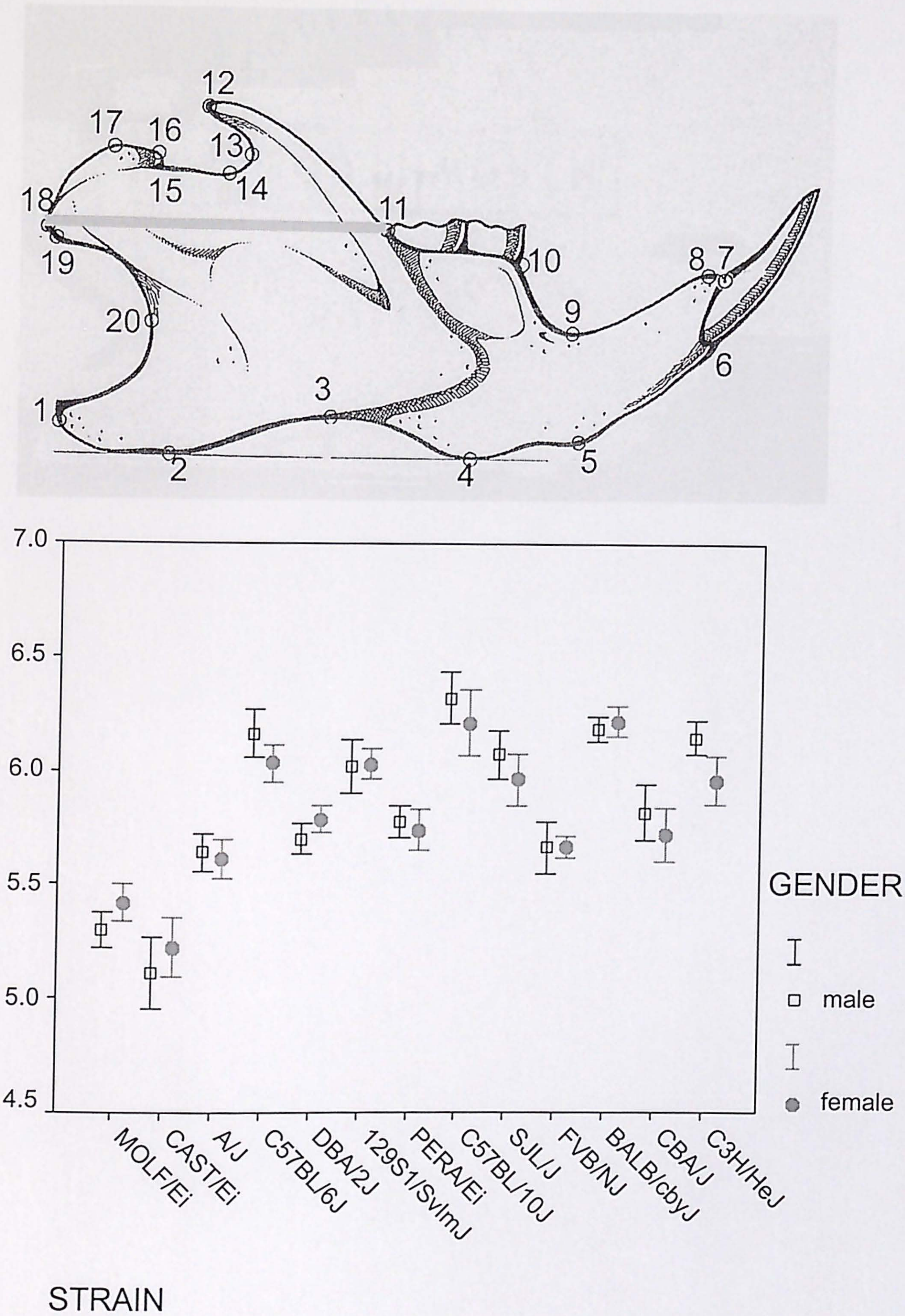


FIGURE 15. Variable 18 Right, Width of Anterior portion of Ramus at Vertical Height equivalent to Distal Surface of the Molar. Upper panel shows buccal view of the right hemi-mandible. Landmarks 11 and 18 determined variable 18. Lower panel shows the length of variable 18 in mm (±2 SEM). Strains are arranged according to body weight (FIGURE 3). Males = open squares, and females = solid circles.

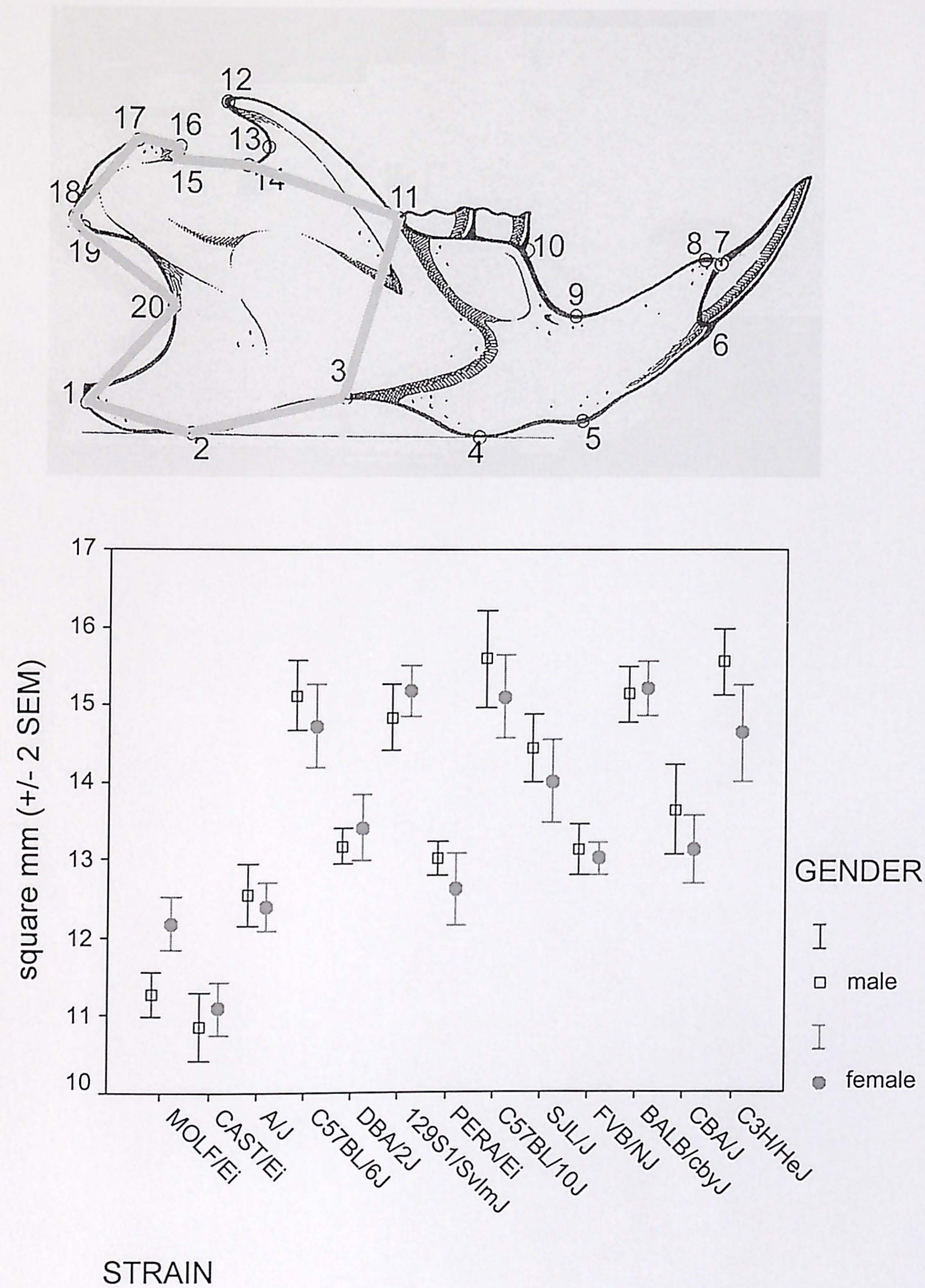


FIGURE 16. Variable 19 Right, Area of Posterior Mandible. Upper panel shows buccal view of the right hemi-mandible. Landmarks 1, 2, 3, 11, 14, 15, 16, 17, 18, 19 and 20 determined variable 19. Lower panel shows the area of variable 19 in mm^2 ($\pm$2 SEM). Strains are arranged according to body weight (FIGURE 3). Males = open squares, and females = solid circles.

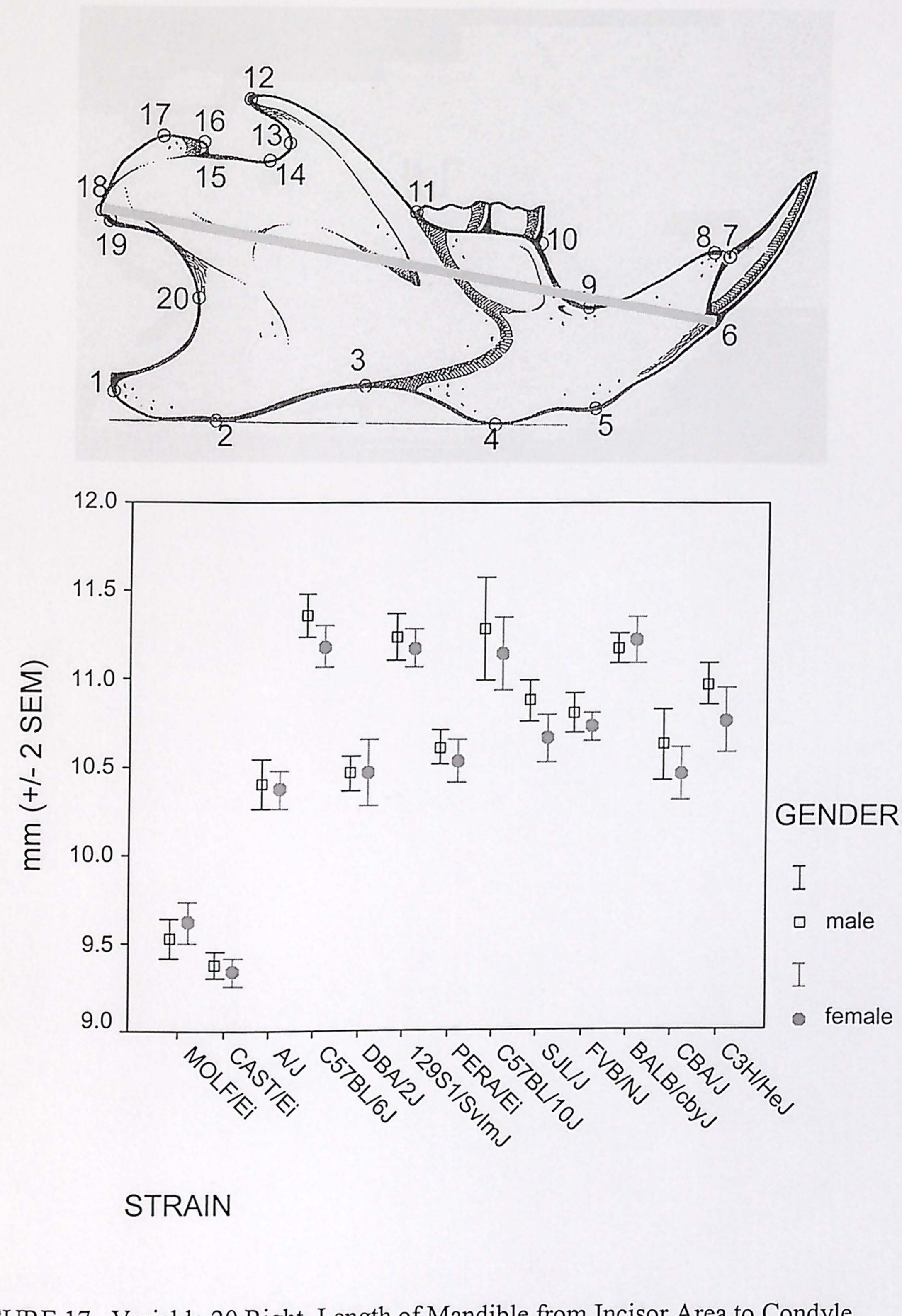


FIGURE 17. Variable 20 Right, Length of Mandible from Incisor Area to Condyle. Upper panel shows buccal view of the right hemi-mandible. Landmarks 6 and 18 determined variable 20. Lower panel shows the length of variable 20 in mm (±2 SEM). Strains are arranged according to body weight (FIGURE 3). Males = open squares, and females = solid circles.

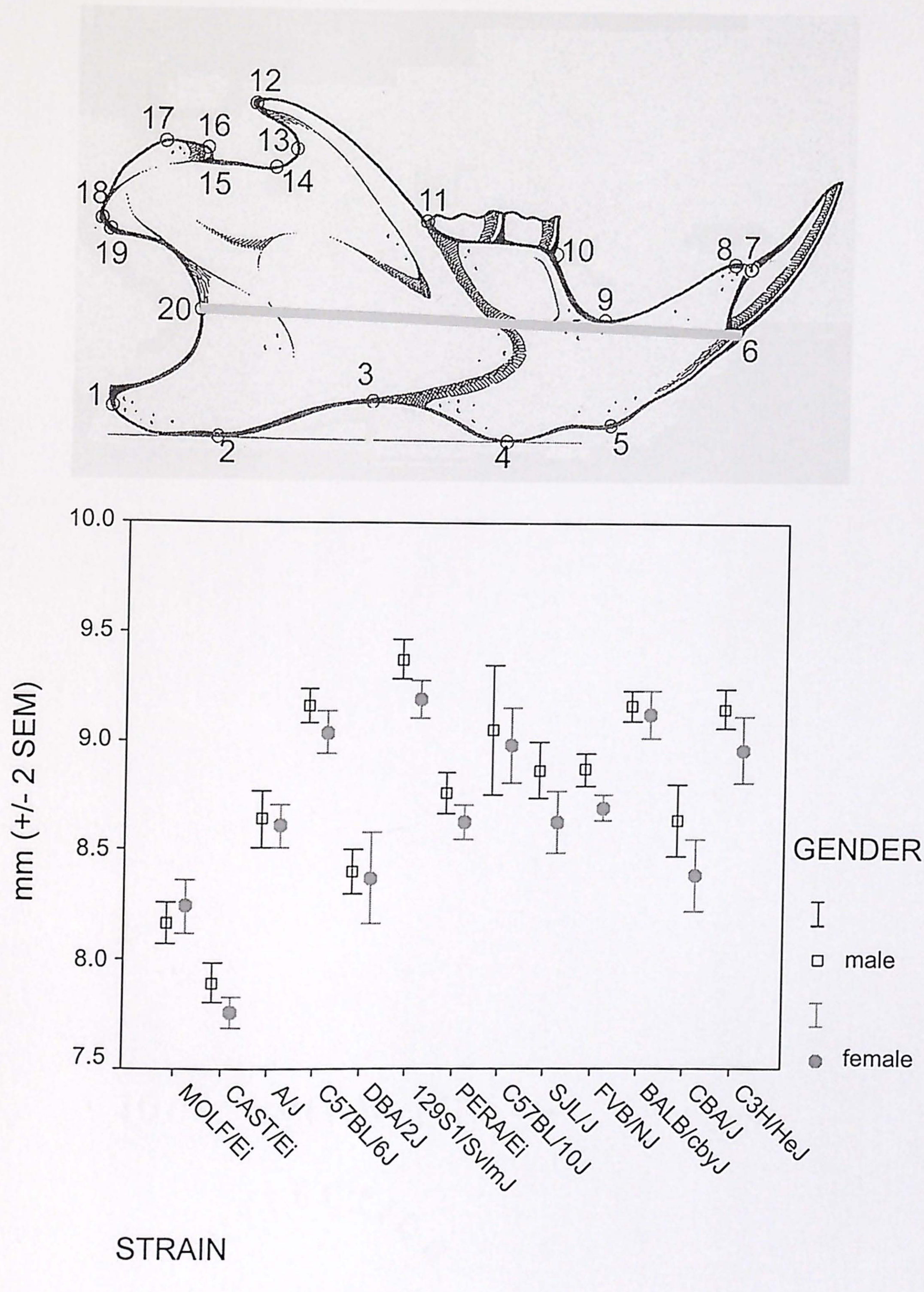


FIGURE 18. Variable 21 Right, Length of Incisor Area to Midpoint Convexity of Area Between Condylion and Angular Process. Upper panel shows buccal view of the right hemi-mandible. Landmarks 6 and 20 determined variable 21. Lower panel shows the length of variable 21 in mm (±2 SEM). Strains are arranged according to body weight (FIGURE 3). Males = open squares, and females = solid circles.

DISCUSSION

Our central hypothesis was that inbred strains of mice exhibit distinguishing morphological mandibular traits. The following null hypothesis was put forward: "There were no differences in morphological mandibular traits between the collection of inbred strains to be examined." In other words, the suite of quantitative bilateral mandibular traits will fail to distinguish mice originating from genealogically separate inbred strains. We were able to reject the null hypothesis.

The objective of this project was to determine and measure differences in quantitative morphologic variables within and between different inbred mouse strains and to assess elements of sexual dimorphism through bilateral measurements of the hemi-mandibles. It was through careful morphometric analysis of mandibular structures within and between inbred strains of mice that quantifiable differences were identified. We anticipated that following analyses of the mandibular traits, sub-groups of traits (variables) could be identified as being able to discriminate individuals between and within strains. Ideally, this subset of traits would form the cornerstone for future genetic studies. Those genetic studies could investigate through quantitative trait loci (QTL) mapping regions of the mouse genome that contribute to normal variation in craniofacial development and morphogenesis. If successful, this will serve as a first step in furthering our understanding of the genetic and environmental components that determine craniofacial form.

It is logical to think increased body weight would be indicative of increased body size. The ordered strains of lightest to heaviest body weight were applied consistently to all the variables measured to more clearly demonstrate if a mouse that belonged to a small or lightweight class had a small or large skeletal characteristic. It would more clearly compare intra- and inter- strain differences in the variables measured.

In Atchley's study,[30] the largest phenotypic correlations with body weight are found in the tooth-bearing area, posterior mandible height, anterior mandible height, and ramus height. These traits are strongly affected by increasing body weight during the prenatal and early postnatal development.[30]

VERTICAL

The variables (4 and 16) that measured mandible height were significantly correlated to body weight. A generality could therefore be drawn that mice that weigh less tend to have smaller skeletal structures. The two smallest strains, CAST/Ei and MOLF/Ei, both have small body weight and short mandibles.

However, the height of the mandible shows a fairly wide intra-strain variance, especially the DBA/2J strain. The FVB/NJ strain is classified as a heavy-weighted mouse and has a short vertical height of the posterior mandible comparable to the small mice MOLF/Ei and CAST/Ei. This is an example of a large mouse with a heavy body weight having a small skeletal variable similar to the small mice. Thus, it is not always true that a small mouse will have small dimensions in all the skeletal areas where a large mouse will have large dimensions.

Vogl[18] analyzed the postnatal ontogeny of the mandible of two inbred strains (C3HeB and C57BL/6) and discovered that regions that discriminate best between the two strains change during development. At 10 to 20 days postnatal age, the coronoid process separated the groups clearly. As ontogeny progressed at 25 days postnatal age, the masseter area discriminated the best.[18] This could be due to the increasing presence of functional muscles that stimulate bone growth.[18] Six area traits of the mandible were studied. The areas were the angular, condylar, coronoid, masseter, and posterior alveolar and anterior alveolar areas.

HORIZONTAL

Variable 1 measured the length of the posterior part of the mandible. The length of the posterior mandible appeared to be closely related to body weight. There are three distinct subgroups much like the subgroups found in the body weight variable. The small mice have the smallest posterior mandible length, and the members of the heaviest weight group have the longest length of the posterior mandible. Many muscles attach in the area, therefore shaping the posterior mandible. The larger the mouse, the heavier and quite possibly the more active the muscles are.

The mechanical loading of muscles on bones at the site of attachment influences skeletal morphology.[28] The face and mandible exhibit more differences in later growth because of the increased influence of muscles on these regions as growth continues.[28]

Variable 7 is an example of functional anatomy. Females in this respect appear to be larger in absolute terms at the widest part of the condyle than males for seven of the 13 strains. Perhaps the female mouse needs more nourishment than the male and uses its muscles more, thus increasing the size of this trait.

AREA

CAST/Ei and MOLF/Ei have the smallest anterior and posterior areas of the mandible. The other strains seem to be comparable in this dimension. In this instance, CAST/Ei and MOLF/Ei mice have the smallest skeletal variable measured in mm.[2] It could be that smaller mice need less food to sustain them, thus decreasing their need for using the muscles involved in the power stroke of mastication.

The results of this project demonstrate that size defined by body weight is not always proportional to skeletal traits. It appeared that the smallest two strains by body weight are consistently small in skeletal traits. CAST/Ei and MOLF/Ei were repeatedly small in size measured by body weight and small in their skeletal structures overall. However, the mid- and larger- body weight mice can have smaller structures comparable to the small-weighted mice or larger skeletal structures. There was not a strong pattern in the mid- and heavy- weighted mice to skeletal size as there was for MOLF/Ei and CAST/Ei.

The study by Vogl et al.[18] suggested that the development of morphometric differences do not proceed smoothly and continuously. The unpredictable pattern of the development of the mandible is expected if epigenetic and regulatory processes integrate it.

Moss' Functional Matrix Theory can be used to at least partially explain the results of this study. It suggests that stimuli coming from the growth and the actions of multiple sources within the growing head and body directly or indirectly function to turn on or off cellular activity. Thus, growing and changing custom-fitted bones are constantly changing and updated to accommodate the changing developmental conditions to make an interrelated system.[26]

SEXUAL DIMORPHISM

Sexual dimorphism occurs when there are differences in the male and female body due to sexual maturation and includes secondary sex characteristics. Sex hormones can affect gene expression leading to sexual dimorphism.[1]

Across these 13 inbred mouse strains, there are some variables with a distinct difference between males and females and other variables that are similar. Body weight as a variable demonstrates a distinct trend for an increase in males compared with females across all strains. It is also evident in this study that the larger the mouse, the larger the difference between males and females is in respect to body weight.

In the C57 and the C3H strains of mice in Vogl's study, male mice were 5 to 10 percent heavier than female mice.[18] Males were generally larger in most other variables measured, especially in body weight and the area of the anterior mandible.

Sex hormones and other factors can affect gene expression leading to sexual dimorphism. In the study by Vogl, the morphology of the mandible responds differently to male and female hormonal environments. It was found that all mandibular traits at 25 days of age showed sexual dimorphism in C3H mice.[18]

Gender was compared within each inbred mouse strain in the present study for the right side and left side measurements for each variable. The A/J and DBA/2J males and females are the most alike in all of the variables measured. The strain with the most variability between males and females is C3H. The second most variable strain between the sexes was CBA/J. It could be surmised that mice in the A/J and DBA/2J strains of males and females could be used in any future study of interest that needed low sexual dimorphism for mandibular morphology. If the males and females in those strains are most alike, there could be a discriminating trait found secondary to an external factor. For example, a researcher may need two strains in which males and females are most alike to study an effect of a drug or environmental stress on a certain trait that affects males and females differently.

Looking at the left side and right side separately could also reveal sexual dimorphism. Again, the DBA/2J and A/J strain were most similar between males and females for the left and the right sides. This suggests that DBA/2J and A/J could be developmentally stable strains of mice. Therefore, it appeared that the particular side studied is not important.

The variable that had the greatest number of significant differences between males and females is variable 3, which is the horizontal length of the mandible measured from the angular process. The angular process is an area of the mandible with many muscle attachments. Teeth, processes that provide leverage, and muscle attachment sites have often had their relative sizes, shapes, and locations on the mandible drastically change.[27] When mice begin to eat solid food, their power stroke of mastication is larger, thus affecting the shape of their mandible.

Variables are not in sequential order due to some broken landmarks on the mandible during data collection or duplicate variables.

SUMMARY AND CONCLUSION

Phenotypic differences make inbred strains of mice exceptional tools for the dissection of genetic factors that govern normal and abnormal craniofacial morphogenesis. While numerous investigations have focused on abnormal morphogenesis, few studies have investigated normal craniometric morphology across multiple inbred strains. The Mouse Phenome Project, an international collaboration of investigators, was formed to systematically phenotype a collection of normal inbred mouse strains.

The objective of the proposed research was to determine and measure differences in quantitative morphologic variables within and between different inbred mouse strains and to assess elements of sexual dimorphism through bilateral measurements of the hemi-mandibles. It was through careful morphometric analysis of craniofacial structures within and between inbred strains of mice that quantifiable differences were identified. Our central hypothesis was that different inbred strains of mice exhibit distinguishing morphological mandibular traits. The following null hypothesis was put forward: "There were no differences in morphological mandibular traits among the collection of inbred strains to be examined." Data from this study allow us to reject our null hypothesis.

Ordering body weight of all the strains from smallest to largest allowed for grouping stains into three weight classes. Also, measured traits could be compared relative to body size. Overall, CAST/Ei and MOLF/Ei were consistently small in size measured by body weight with small skeletal structures. There was no strong pattern in the mid- and heavy- weighted mice to skeletal size. It was shown that some strains of mice that were larger according to body weight had a small skeletal structure. For example, the FVB/NJ strain had a short vertical height of the posterior mandible comparable to small strains. Thus, it is not always true that a small mouse will have small dimensions in all the skeletal areas where a large mouse will have large dimensions.

Evidence of sexual dimorphism was supported. Overall, it appears males and females that have the least significant difference between them are in the DBA/2J strains, followed by A/J. The strain with the most significance difference between males and females is the C3H/HeJ strain.

The variable that showed no significant difference between males and females ($p < 0.05$) is variable 2, which is the horizontal length of the posterior mandible. This variable was not significantly different in the total, left side, and right side measurements of the mandible. The variable that had the greatest significant difference between males and females is variable 3, which is the horizontal length of the mandible measured from the angular process. Overall, strains do differ significantly across most variables.

These differences have allowed us to identify a subset of traits that discriminate and classify the strains and set the stage for future genetic studies that will search for genes that contribute to determining craniofacial form.

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ABSTRACT

NORMAL MANDIBULAR MORPHOLOGY OF INBRED MOUSE STRAINS

by

Michelle Halum Edwards

Indiana University School of Dentistry

Indianapolis, IN

Even though the molecular events and pathways that underlie craniofacial development and morphogenesis are not fully understood, it is accepted that their orchestration is influenced by the interaction of genetic and environmental factors. Inbred mouse strains represent genetically homogenous groups of individuals. It is established that mice in one strain often differ quite remarkably from mice in other inbred strains. Those phenotypic differences make mice exceptional tools for the dissection of genetic factors that influence normal and abnormal craniofacial morphogenesis. While numerous investigations have focused on abnormal morphogenesis, a comprehensive study of normal craniometric morphology across multiple inbred strains of mice has not been previously performed. The Mouse Phenome Project, an international collaboration of investigators, was formed to systematically phenotype a collection of normal inbred mouse strains. The objectives of our studies were to determine and measure differences.

in quantitative mandibular traits/variables within and between different inbred mouse strains, and to assess sexual dimorphism through bilateral measurements of the hemimandibles. These studies were a component of the Mouse Phenome Project to collect normal craniometric data from 12 genetically heterogeneous inbred strains utilizing digital images from equal numbers of female and male mice at 7to 8 weeks of age.

Our central hypothesis was that morphometric analysis of mandibular structures from genetically disparate inbred mouse strains would reveal quantifiable differences. The null hypothesis of no difference among the strains for mandibular measurements was rejected. Overall, CAST/Ei and MOLF/Ei were consistently small in size measured by body weight with small skeletal structures. There was no strong pattern of body weight and site of skeletal size in the mid and heavy weighted strains.Evidence of sexual dimorphism was supported. Overall, it appears males and females that have the least significance between them are in the DBA/2J strain, followed by A/J. The strain with the most significant difference between males and females is in the C3H/HeJ strain.

CURRICULUM VITAE

Michelle Halum Edwards

December 17, 1970	Born in Hammond, Indiana
December 1993	BA, Psychology, University of South Carolina, Columbia, South Carolina
May 1997	Post-Bachelor, Indiana University Northwest, Gary, Indiana; Loyola University, Chicago, Illinois, and Purdue Calumet, Hammond, Indiana
May 2001	DDS, Indiana University School of Dentistry, Indianapolis, Indiana
June 2003	Certificate, Pediatric Dentistry, Indiana University School of Dentistry, Indianapolis, Indiana

Professional Affiliations

American Dental Association
American Academy of Pediatric Dentistry
Indiana Dental Association
Indiana Society of Pediatric Dentistry

Certifications

Basic Life Support
Pediatric Advanced Life Support
Invisilign
Board Eligible of American Academy of Pediatric Dentistry